Metal-salen catalysts in the oxidation of lignin model compounds

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Academic Dissertation

To be presented, with the permission of the Faculty of Science of the University of Helsinki, for public criticism in the Auditorium A129 of Chemicum, A. I. Virtasen Aukio 1, on 21st of June, 2005 at 12 noon.

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ISBN 952-91-8775-0 (bound)

ISBN 952-10-2493-3 (PDF)

http://ethesis.helsinki.fi

Abstract

Salen complexes are an important class of coordination compounds, which have been used to catalyse a wide variety of reactions. Many of these reactions are oxidations of organic substrates with terminal oxidants. Dioxygen and hydrogen peroxide are desirable terminal oxidants from both the economical and environmental points of view.

The oxidation of lignin model compounds can provide us with information on the reactivity of both the model compounds and lignin itself and assist in the development of new catalysts for pulp bleaching processes that do not rely on chlorine-containing chemicals. Model compound studies can also help us to understand the fuctioning of the lignifying and delignifying enzymes present in nature.

New salen-type complexes of the first-row transition metals cobalt, copper, iron, manganese and nickel were synthesised and characterised. Their catalytic properties were then evaluated in the oxidation of lignin model compounds and of other selected substrates, such as 2,4,6-trichlorophenol and benzylic hydrocarbons. Both dioxygen and hydrogen peroxide were employed, in addition to other oxidants. Lignin precursor coniferyl alcohol was found to undergo oxidative coupling, yielding products with different degrees of polymerisation. With hydrogen peroxide as oxidant, benzylic alcohols were selectively oxidised to the corresponding aldehydes and ketones. A mechanism for the oxidation of phenolic benzylic alcohols was postulated. The catalysts that were developed could suitably be used in “green” synthetic procedures and as simple models for oxidative enzymes present in nature.

"Every man is one star"

Ior Bock

Preface

The experimental work for this thesis was carried out in the Laboratory of Organic Chemistry of the University of Helsinki during the years 1998-2001. The literature study was done in 2005.

I am indepted to my supervisor, Docent Jussi Sipilä, for guiding me into the field of lignin chemistry and biomimetic oxidation and for his support and encouragement. I am grateful to Dr. Pekka Pietikäinen for introducing me salen-type chemistry and for his cooperation and many fruitful discussions.

Professor Emeritus Tapio Hase and Professors Mikko Oivanen and Kristiina Wähälä, past and present heads of the Laboratory of Organic Chemistry, kindly placed the research facilities of the Laboratory at my disposal.

I wish to thank Professor Markku Leskelä, Head of the Laboratory of Inorganic Chemistry, for his kindness and encouragement. Thanks go as well to Docents Ilpo Mutikainen and Timo Repo of the Laboratory of Inorganic Chemistry for a productive collaboration, endless discussions and unfailing support. Docent Ilpo Mutikainen is especially thanked for processing the .cif-files for graphical presentation. Professor Emeritus Aarne Pajunen is thanked for the crystallographic work and Dr. Jorma Matikainen for running the EI mass spectra.

My colleagues, in and out of the Laboratory made an invaluable contribution through their help and wide-ranging conversation.

Finally, I thank my gradmother Lyyli for being present in spirit, my parents Eira and Aimo for their continuous support and their faith in me during these long and hard years of work. My sincerest appreciation goes to my beloved wife Pia-Minna for her endless love and patience and having the fortitude to stay by my side. And little Onni-Ilmari, thank you for being the sunshine of my life.

Tuusula, April 2005

Anssi Haikarainen

List of original publications

This thesis is based on the following original publications, which are referred to in the text by Roman numerals I-VI.

I A. Haikarainen, J. Sipilä, P. Pietikäinen, A. Pajunen and I. Mutikainen: "Synthesis and characterization of bulky salen-type complexes of Co, Cu, Fe, Mn and Ni with amphiphilic solubility properties" *J. Chem. Soc., Dalton Trans.*, 2001, 991.

II A. Pajunen, I. Mutikainen, A. Haikarainen, J. Sipilä and P. Pietikäinen: "{2,2'-[(*R*,*R*)-cyclohexane-1,2-diylbis(nitrilomethylidyne)]bis[6-*tert*-butyl-4-(triphenylphosphoniomethyl)phenolato]-*O*,*N*,*N'*,*O'*}copper(II) dichloride hexakis(deuterochloroform) solvate" *Acta Cryst. Sect. C: Cryst. Struct. Commun.*, 2000, **C56**, E321.

III A. Pajunen, I. Mutikainen, A. Haikarainen and J. Sipilä: "Crystal structure of chloro{2,2'-[(*R*,*R*)-cyclohexane-1,2-diylbis(nitrilomethylidyne)]-bis[6-*tert*-butyl-4-(triphenylphosphoniomethyl)phenolato]-*O*,*N*,*N'*,*O'*}-iron(III) bis(hexafluorophosphate) tris(ethanol) solvate, $[Fe(C_{66}H_{68}N_2O_2P_2)Cl](PF_6)_2 \cdot 3C_2H_6O$" *Z. Kristallogr. NCS*, 2001, **216**, 147.

IV A. Haikarainen, J. Sipilä, P. Pietikäinen, A. Pajunen and I. Mutikainen: "Salen Complexes with Bulky Substituents as Useful Tools for Biomimetic Phenol Oxidation Research" *Bioorg. Med. Chem.*, 2001, **9**, 1633.

V A. Pajunen, G. Brunow, A. Haikarainen, P. Pietikäinen and J. Sipilä: "Crystal structure of bis{[μ_2-*N*,*N'*-ethylenebis(salisylideneaminato)]-manganese(II)}, $C_{32}H_{28}Mn_2N_4O_4$" *Z. Kristallogr.–New Cryst. Struct.*, 1998, **213**, 441.

VI J. Sipilä, A. Haikarainen, P. Pietikäinen, G. Brunow, T. Repo, J. Anturaniemi and M. Leskelä: "Metal-Schiff Base Complexes: Useful Mimics for Phenol Oxidants in Catalytic Delignification?" *ACS Symp. Ser.*, 2001, **785**, 286.

Contents

Abbreviations

Ac	acetyl
ATR	attenuated total reflection
$[bmim]^+$	1-butyl-3-methylimidazolium cation
DMF	dimethylformamide
EI	electron impact ionisation
ESI	electrospray ionisation
Et_2O	diethylether
EtOH	ethanol
EPR	electron paramagnetic resonance
Him	imidazole
HRMS	high resolution mass spectrometry
IR	infra red
LiP	lignin peroxidase
Me	methyl
MeO	methoxy
MeOH	methanol
MnP	manganese peroxidase
MS	mass spectrometry
MW	molecular weight
N-Me-salprH_2	2,2'-[(methylimino)bis(3,1-propanediylnitrilomethylidyne)]bis-phenol
NMR	nuclear magnetic resonance
salbnH_2	2,2'-[1,4-butanediylbis(nitrilomethylidyne)]bis-phenol
salenH_2	2,2'-[1,2-ethanediylbis(nitrilomethylidyne)]bis-phenol
salophenH_2	2,2'-[1,2-phenylenebis(nitrilomethylidyne)]bis-phenol

salprH_2	2,2'-[iminobis(3,1-propanediylnitrilomethylidyne)]bis-phenol
sulfosalenH_2	2,2'-[1,2-ethanediylbis(nitrilomethylidyne)]bis[4-sulfonatophenol] disodium salt
THF	tetrahydrofuran
TON	tunrnover number
UV	ultraviolet
Vis	visible

1. INTRODUCTION

Salen-type complexes are a fundamental class of compounds in coordination chemistry, known since 1933.[1] They have been extensively studied and more than 2500 have been synthesised.[2a] Interest in salen-type complexes intensified in 1990 when the groups of Jacobsen[3] and Katsuki[4] discovered the enantioselective epoxidation of unfunctionalised alkenes using chiral Mn(salen) complexes as catalysts. Since that time, an extremely wide variety of reactions catalysed by salen complexes has been investigated. These include oxidation of hydrocarbons,[5] aziridination of alkenes,[6] Diels-Alder reaction,[7] hydrolytic kinetic resolution of epoxides,[8] alkylation of aldehydes[9] and oxidation of sulfides to sulfoxides[10].

Traditional methods for the oxidation of organic substrates involve the use of stoichiometric amounts of high-valent metal compounds, such as CrO_3. Unfortunately these kinds of reactions generate huge amounts of toxic waste and are becoming less popular in the face of growing environmental concerns.[11] Besides being environmentally more bening, catalytic oxidation of organic compounds with oxidants such as dioxygen and hydrogen peroxide is less economically wasteful than the traditional methods and is now an important reaction in both research laboratories and industry.[12, 13]

Salen-catalysed oxidations of organic compounds have been widely studied. Indeed, the asymmetric epoxidation of alkenes has reached the stage where it is used in industrial, multi-ton scale preparation of the HIV protease inhibitor Indinavir (marketed as Crixivan by Merck).[14, 15] But there remain many areas where selectivity and catalyst stability, activity and recyclability need to be improved before the reactions are suitable for the synthesis of fine chemicals.

Oxidation of phenols is an important reaction because the benzoquinones that are produced are important starting materials for a diversity of compounds, including pharmaceuticals. Phenols can also be oxidised to high-performance polymeric materials such as crystalline poly(1,4-phenyleneoxides).[16] The oxidation of benzylic alcohols is important in fine chemicals manufacturing. The carbonyl compounds that are produced, most notably aldehydes, are used in large quantities as flavours, fragrances and pharmaceuticals, or in the synthesis of the aforementioned products.

Catalytic oxidation of lignin offers a way to produce fine chemicals, such as vanillin. These methods are not yet economically feasible, however. Catalytic lignin oxidation also could make pulp bleaching more environmentally friendly and more cost effective. Model compound studies that enable us to better understand oxidative transformations and to obtain more efficient catalysts are key to developing these strategies.

In the experimental part of this work, a series of salen-type transition metal complexes were synthesised and characterised with the aim of developing efficient and easily prepared oxidation catalysts. The new complexes were then used to catalyse the oxidation of organic compounds related to lignin, when hydrogen peroxide and dioxygen were applied as oxidants in aqueous media. These oxidants and solvent systems were chosen because they are cheap and environmentally benign, falling within the area of “green chemistry”.

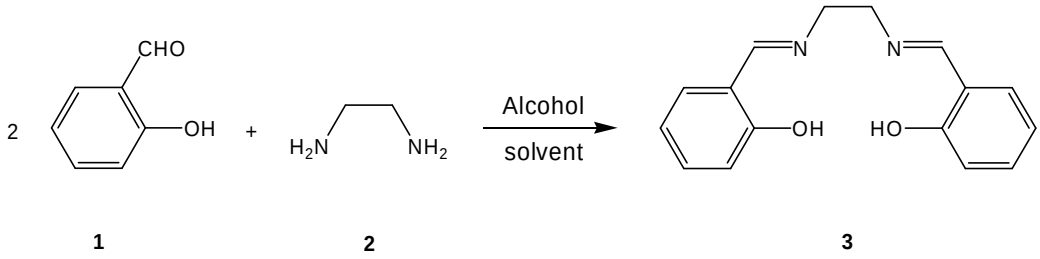
In the literature review that follows I discuss the chemistry of metallosalen complexes, including some rarer subclasses, their chemistry with oxygen-derived ligands and finally their use as catalysts in oxidations of phenolics, benzylic alcohols and lignin model compounds. The syntheses undertaken as part of this work are summarised in sections **5.1**–**5.3** and in more detail in chapter 7,

Experimental. The results of tests of these new complexes in catalytic oxidations of coniferyl alcohol, benzylic alcohols and more complex lignin model compounds are reported in sections **5.4**–**5.6**. An analysis of the electronic effect of the catalyst in the reaction rate in the oxidation of 2,5-di-*tert*-butylhydroquinone is presented in section **5.7** and the results of other oxidations are reported in section **5.8**. A full description of the work can be found in papers I–VI, which are attached as appendices.

2. SALEN-TYPE COMPLEXES

2.1. General aspects of salen complexes

The first salen-type Schiff base metal complexes were synthesised in 1933 by condensing salicylaldehyde and ethylenediamine with various metal salts by a one-pot method. Most of the products were brightly coloured solids, with the colour dependent on the metal.[1] Later it became customary first to prepare the organic salen ligand and then to complex it with the desired metal salt. The standard method for the preparation of the ligand has been and still is the condensation of salicylaldehyde or its derivative with ethylenediamine or its derivative in alcohol solvent, usually ethanol or methanol (Scheme 1).[17, 18]



Scheme 1 Synthesis of basic salen structure.

In this way the ligands are often obtained as relatively pure crystalline solids directly from the reaction mixture. The complexation reaction with metal salt is also usually performed in alcohol

solvent, unless the reactivity of the starting materials or the product prohibits this. Salen complexes with main-group metals tend to be particularly air- and moisture-sensitive and must be handled appropriately. Inert atmospheres and suitable solvents such as anhydrous THF or toluene can be used.[19] Quantities of the ligand and the desired metal salt may be equimolar, or metal salt can be used in excess. When the desired complex is soluble in organic solvents, an excess of the metal salt is typically used to drive the reaction to completion, and the remainder of the salt is removed by washing with water. Excess salts can also be removed *via* chromatographic techniques.

The metal complexes can be purified by recrystallisation, and sometimes by column chromatography unless they are easily degraded. Often they are highly coloured solids, the colour depending on the central metal ion. The transition metal complexes of salen ligands typically exhibit particularly bright colours, such as green, brown to black, deep purple, red and orange-brown. Titanium, zirconium and zinc complexes are usually lightly coloured, most often pale yellow, as are the complexes with main-group metals.

Several review articles and books deal with the synthesis and applications of salen complexes.[2, 17, 18, 20–25] This great interest in salen complexes began with the discovery by Jacobsen[3] and Katsuki[4] in 1990 of the enantioselective epoxidation of unfunctionalised alkenes with chiral salen complexes as catalysts. To date over 2500 metal complexes of salen-type ligands have been synthesised and characterised and they constitute a fundamental class of compounds in coordination chemistry.[2a] Table 1 lists some reactions other than oxidations reported from 2004 to March 2005. The catalytic activity of salen complexes has been studied in a wide variety of reactions during the last two decades.[26, 27] Epoxidation of alkenes can be described as an “established industrial procedure”. For example, in the industrial multi-ton-scale synthesis of the HIV protease inhibitor Indinavir **4**

(marketed as Crixivan by Merck), the key building block, (1*S*,2*R*)-1-amino-2-indanol, is prepared from indene by asymmetric epoxidation using "Jacobsen's catalyst" **5**[28] (Fig.1) and NaOCl.[14]

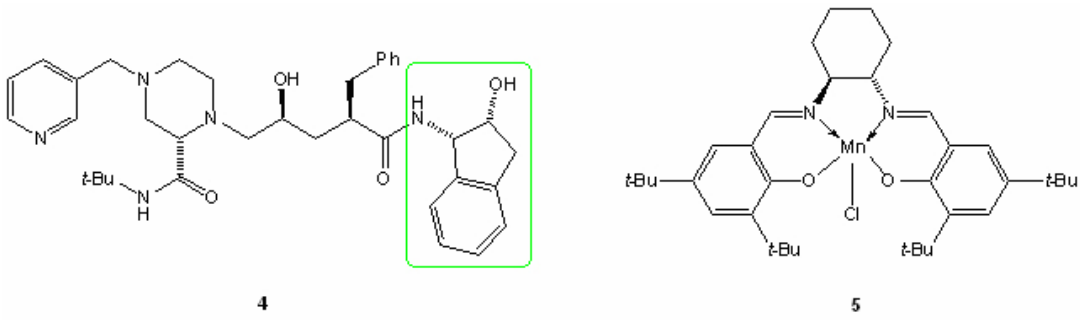
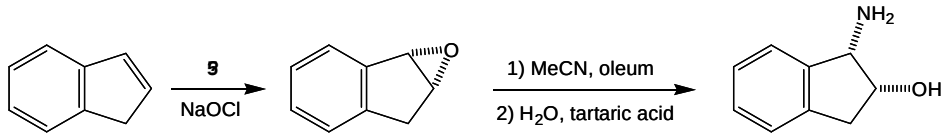


Fig. 1 HIV protease inhibitor Crixivan **4** [(1*S*,2*R*)-1-amino-2-indanol moiety highlighted] and "Jacobsen's catalyst" **5**.

The chiral epoxide is then subjected to Ritter reaction. The epoxide behaves like a diol in this reaction with acetonitrile and oleum to yield the target *cis*-aminoindanol (Scheme 2).[15] An earlier method for the synthesis of (1*S*,2*R*)-1-amino-2-indanol consisted of formation of the epoxide intermediate as a racemate, followed by Ritter reaction, and finally resolution of the (±)-aminoindanol with tartaric acid. This earlier method is clearly inferior to the contemporary salen-catalysed process, being both more laborious and wasting half of the racemic aminoindanol.



Scheme 2 Industrial synthesis of enantiomerically pure (1*S*,2*R*)-1-amino-2-indanol, building block of Crixivan.

Table 1 Examples of salen-catalysed reactions published between 2004 and March 2005.

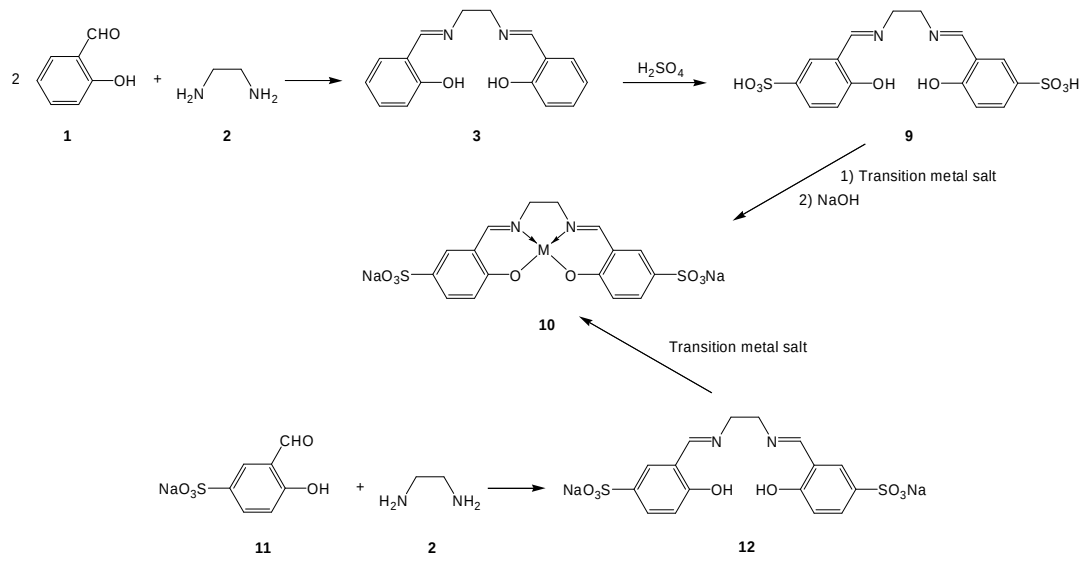
Reaction	Metal in the catalyst	Ref.
Hydrolytic kinetic resolution of terminal epoxides	Co^{3+}	8
Asymmetric addition of Et_2Zn to aldehydes	Zn^{2+}	9
Asymmetric aziridination of alkenes	Ru^{2+}	6
Asymmetric allylation of alkyl glyoxylates	Cr^{3+}	29
Asymmetric conjugate addition of carbon- and nitrogen-based nucleophiles to α,β-unsaturated ketones	Al^{3+}	30
Asymmetric Meerwein-Ponndorf-Verley cyanation of aldehydes	V^{5+}	31
Asymmetric addition of ethyl cyanoformate to aldehydes	Ti^{4+}	32
Asymmetric Hetero-Diels-Alder reaction	Co^{2+}, Cr^{3+}	33
Cross-coupling of aryl Grignards with alkyl halides	Fe^{3+}	34
Asymmetric aminolysis of epoxides	Cr^{3+}	35
Synthesis of biodegradable polyesters and polycarbonates	Al^{3+}	36
Asymmetric Diels-Alder reaction	Co^{3+}	7
Asymmetric alkylation of indoles	Al^{3+}	37
Formal asymmetric hydration of α,β-unsaturated imides	Al^{3+}	38

2.2. Water-soluble salen complexes

Most of the salen complexes synthesised to date have been nearly insoluble in water because the ligand has not contained sufficiently polar or ionic groups. The first three syntheses of water-soluble salen complexes were published in 1955[39, 40] and in 1956.[41] The first two papers[39, 40] described the syntheses of various metal complexes of sulfonated salen ligand. The complexes were prepared by first sulfonating the preformed salen ligand with concentrated H_2SO_4, complexing the

produced sulfonic acid derivative of salen with the desired metal salt in EtOH, and finally neutralising the sulfonic acid groups with NaOH to form the disodium salt of the sulfonated complex (Scheme 3). This method is unlikely to produce good quality products in acceptable yields because the imine bonds in the salen structure are sensitive to hydrolysis in acidic conditions and are likely to be destroyed, at least to some extent, by the concentrated sulfuric acid used in the sulfonation step.

The third reference 41, from 1956, describes the synthesis of the same sulfonated complexes but using the sodium salt of the sulfonated salicylaldehyde as a starting material. This aldehyde was condensed with ethylenediamine in EtOH–H_2O to yield the desired ligand directly as disodium salt. After complexing of the ligand with metal salt, the desired products were obtained (Scheme 3). This paper also describes the synthesis of salen derivatives where the salicylaldehyde moieties are replaced by pyridoxalphosphates, likewise yielding water-soluble complexes.



Scheme 3 Two ways to synthesise sulfosalen complexes

Since then, this variation has been used, mainly by Evans and co-workers,[42-44] in the preparation of sulfonated salen complexes and their analogues, which were used for studies on singlet oxygen in aqueous solutions. Co(sulfosalen) complex and its derivatives were prepared in a similar way in 1982, and their reactions with dioxygen were studied.[45] Very recently, a synthesis of chiral Mn(sulfosalen) derivative by the same strategy, and its immobilisation in Zn-Al-layered double hydroxide carrier, was published.[46]

After these few experiments the interest in water-soluble salen complexes seems to have shifted largely to DNA scission and other bioinorganic studies. Several anionic and cationic water-soluble salen complexes have been synthesised for these and other purposes. Almost always, only two types of hydrophilic groups needed for water solubility have been used, either some kind of ammonium group or a carboxylic acid-carboxylate group.[47-49] The crystal structure of the water-soluble dicationic trimethylammonium-substituted Cu(salen) is shown in Fig. 2.

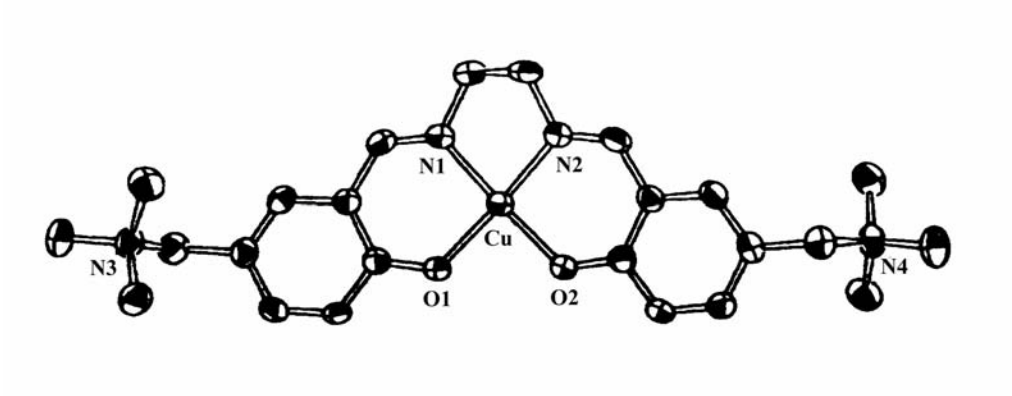


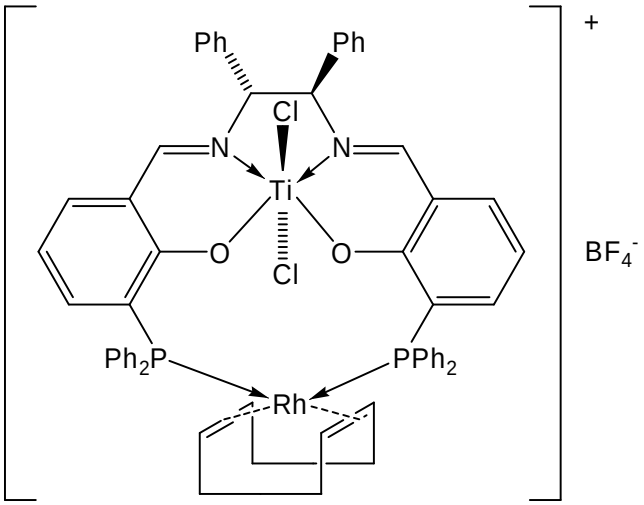
Fig. 2 Crystal structure of the dicationic Cu(salen) derivative. Counterions and hydrogen atoms are omitted for clarity.[47]

Recently vanadylsalen derivatives with tethered imidazolium groups, presumably water soluble, were synthesised and used as catalysts for the cyanosilylation of aldehydes.[50] These complexes were completely insoluble in organic solvents, but were miscible with ionic liquids. A chiral derivative of the complex was used in the enantioselective variation of the reaction.

2.3. Amphiphilic and phosphorus-containing salen complexes

Literature references for salen complexes with amphiphilic solubility properties are extremely few. One reference from 1989 describes the synthesis and properties of an amphiphilic nickel complex of a salen-type ligand.[51] This complex, which was prepared from two subunits, displayed a hydrophobic exterior and a hydrophilic interior. The complex formed micelle-type structures in solution. A recent publication describes some salen complexes bearing triisooctylammonium groups in the ligand framework, but it deals only with the chemistry of these complexes used as epoxidation catalysts after immobilisation in montmorillonite clay, not as homogeneous catalysts.[52] Most likely these complexes exhibit amphiphilic solubility because they were soluble in CH_2Cl_2, despite having ammonium groups. Their solubility in water is most likely limited, however, due to the large alkyl groups attached to the ammonium nitrogen.

No publications mentioning phosphonium-substituted salen complexes were found in a literature search. However, some binuclear phosphine-substituted salen complexes, such as **13**, soluble only in organic solvents, have been synthesised and studied.[53-57] These interesting heterobinuclear compounds contain early- and late-transition metal ions in their N_2O_2- and O_2-coordinating environments, respectively (Fig. 3). Reflecting their salen- and phosphine-type coordination environments, the complexes were given the name salenophos. Their catalytic activity has been studied in the hydroformylation of functionalised alkenes.[57]



13

Fig. 3 Heterobinuclear organometallic Ti^{4+}-Rh^{+}-salenophos complex.[57]

2.4. Salen complexes containing tethered intramolecularly coordinating ligands in addition to the N_2O_2-coordination environment of salen ligand

Many oxidative enzymes, especially peroxidases, containing a haeme prosthetic group in their active site, also contain an axially coordinating ligand. In peroxidases, this is usually a histidine residue of the protein framework, which coordinates to the iron atom, in addition to four nitrogens of the porphyrin macrocycle of the haeme. Examples of such enzymes for which this axially coordinating histidine residue is crucial for proper functioning are horseradish peroxidase (HRP), manganese peroxidase (MnP) and lignin peroxidase (LiP) (Fig. 4).[58-60] Cytochrome P450 enzymes also contain an axially coordinating ligand, in this case the deprotonated cysteinato residue.[61]

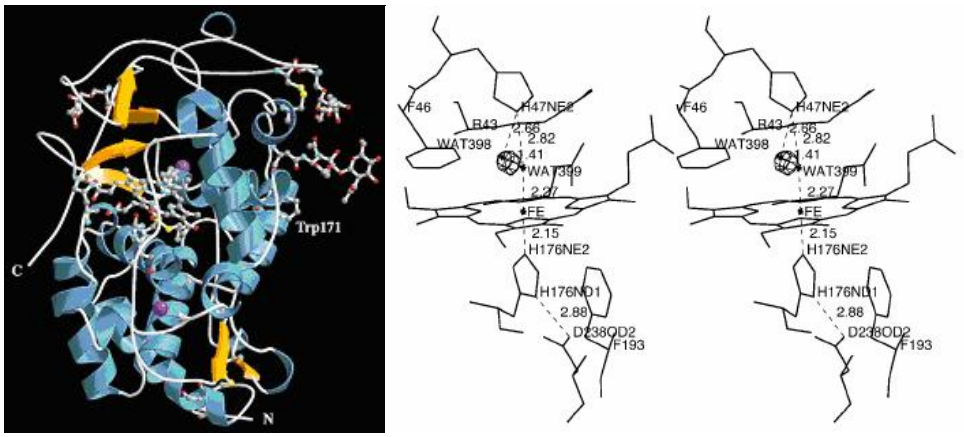
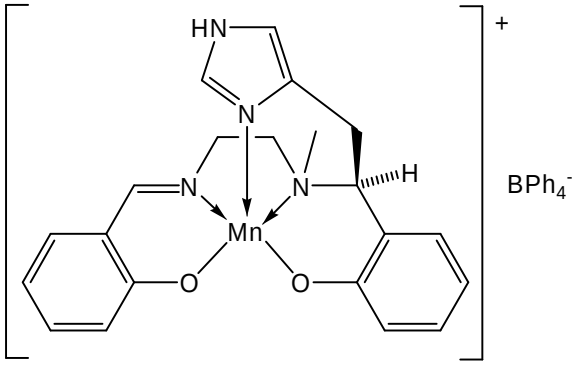


Fig. 4 The overall structure of LiP (left), and a stereo diagram of the active site showing the axially coordinating proximal histidine residue H176NE2 (right). Reprinted from ref. 59, Copyright (1999), with permission from Elsevier.

Knowledge of the structures of the active sites in peroxidase enzymes, in addition to the finding that an added axially coordinating base such as imidazole or pyridine (or a derivative of these) usually greatly increases the reaction rate of salen-catalysed oxidations, most notably epoxidation of alkenes,[62, 63] have encouraged researchers to synthesise salen-type complexes containing this kind of axially coordinating nitrogen base or a *N*-oxide derivative covalently bound in the ligand. In addition, several salen-type complexes containing intramolecularly coordinating alkoxo-[64] amino-[65] carboxylate-[66] or sulfide[67] ligands have been synthesised.

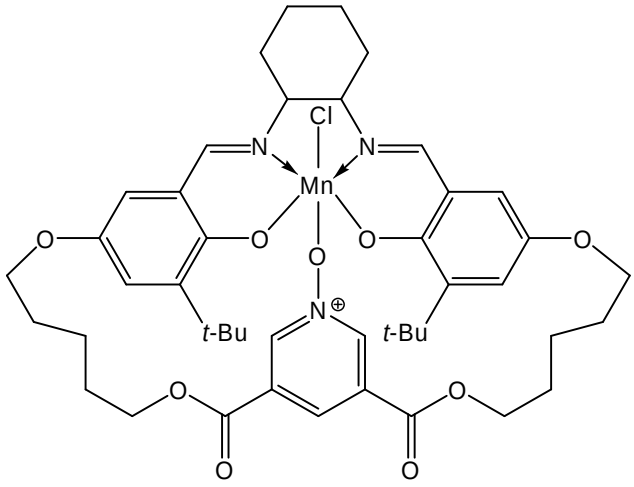
The group of Berkessel[68, 69] has synthesised biomimetic C_2-unsymmetrical Mn^{3+}-dihydrosalen complexes incorporating one imidazole group in the ligand for use as catalysts in asymmetric epoxidation. The imidazole nitrogen is coordinated to the metal in intramolecular fashion leading to N_3O_2-pentacoordinated compounds (Fig. 5). One of the two imine nitrogens in the salen structure is



14

Fig. 5 Biomimetic Mn^{3+}-dihydrosalen complex **14** with intramolecularily coordinating imidazole group.[69]

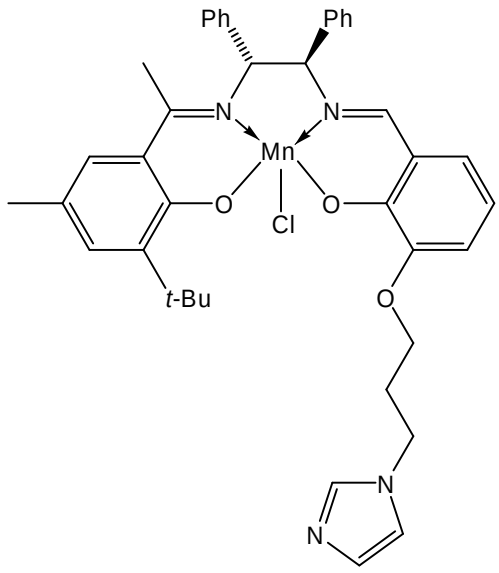
Jacobsen *et al.*[70] synthesised the salen complex **15** containing a coordinating pyridine-*N*-oxide group in the macrocyclic framework of the ligand (Fig. 6). This N_2O_3-coordinating complex was synthesised to obtain some insight into the mechanism of the alkene epoxidation and to rule out the earlier proposed four-membered ring metallaoxetane intermediate (a discussion of the mechanism of the alkene epoxidation catalysed by salen complexes can be found, for example, in ref. 2)



15

Fig. 6 Mn^{3+} complex **15** containing an intramolecularly coordinating pyridine-*N*-oxide group.[70]

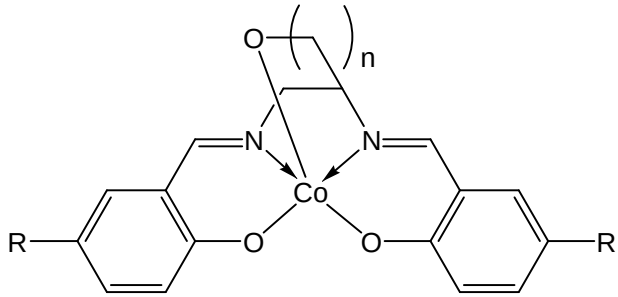
C_2-Unsymmetrical salen-type complex **16** with a tethered imidazole group in the ligand, derived from 1-(2-hydroxyphenyl)-ketone derivative and salicylaldehyde containing the imidazole ligand, has recently been synthesised (Fig. 7).[71] This N_3O_2-coordinating Mn^{3+} complex turned out to be totally inactive in the epoxidation of alkenes, however, presumably due to the strong intermolecular coordination of the imidazole to the Mn^{3+} ions, leading to the formation of a complex dimer where the sixth coordination positions of the metal ions were occupied by chloride anions. This was proposed to inhibit the formation of the active metal-oxo complex.



16

Fig. 7 Mn^{3+} complex derived from 1-(2-hydroxyphenyl)-ketone and salicylaldehyde derivative.[71]

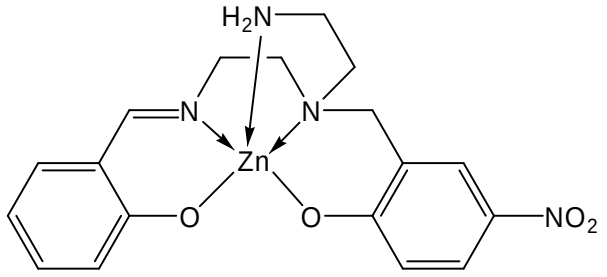
Co^{3+} complexes **17**-**22** containing alkoxo-substituents in the salen ligands (Fig. 8) were studied by van der Baan *et al.* to elucidate the reactions of Co(salen)OH- and Co(salen)-alkoxo species.[64] Initial Co^{2+} complexes were converted to the Co^{3+} complexes shown in Fig. 8 by reacting them with oxygen. Depending on the substitution at 5- and 5'-positions, monomeric or bridged dimeric compounds were obtained.



17 R=H, n=1
18 R=H, n=2
19 R=H, n=3
20 R=*t*-Bu, n=1
21 R=*t*-Bu, n=2
22 R=*t*-Bu, n=3

Fig. 8 Co^{3+} complexes **17-22** with intramolecularly coordinating alkoxo groups.[64]

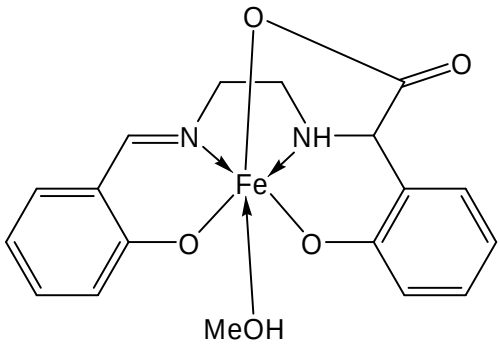
Zn^{2+}-dihydrosalen complex **23** (Fig. 9) was synthesised to mimic phosphatase enzymes in the hydrolysis of bis- and tris(nitrophenyl)phosphates.[65] This complex contains an aminoethyl substituent at the amino nitrogen of the dihydrosalen ligand.



23

Fig. 9 Pentacoordinated Zn^{2+}-dihydrosalen complex **23**.[65]

A model for metalloprotein transferrin, consisting of Fe^{3+} complex of *N*-[2-((*o*-hydroxyphenyl)glycino)ethyl]salicylideneimine (a dihydrosalen derivative) containing a carboxylate group in the amine nitrogen of the ligand, was prepared by Carrano *et al.*[66] (Fig. 10). This complex (**24**) contains a coordinated methanol molecule and the geometry around the Fe^{3+} ion is pseudooctahedral.



24

Fig. 10 Transferrin model, Fe^{3+}-dihydrosalen derivative **24**.[66]

Pentadentate ligand L [2-methyl-4-benzylthio-*N,N'*-butane-1,2-diylbis(salicylideneimine)] and its Co^{3+}, Mn^{3+} and Fe^{3+} complexes were synthesised to investigate the intramolecular coordination of sulfide ligand in salen-type complexes.[67] In the complexes [Co(L)Him]PF_6 (**25**) and [Mn(L)MeOH]BPh_4 (**26**), the sulfur atom coordinates to metal ions in intramolecular fashion (Fig. 11). Interestingly, in the complex [Fe(L)Cl], the pendant sulfide does not coordinate, neither intra- nor intermolecularly.

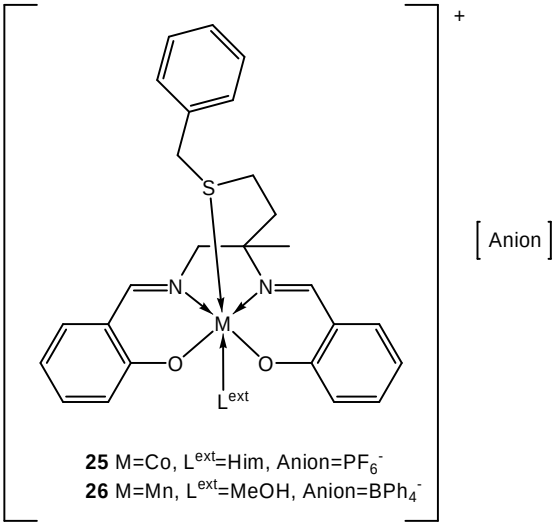


Fig. 11 Complexes **25** and **26** with sulfide pendant arm.[67]

2.5. Structural motifs of metallosalen complexes

The structures of metallosalen complexes range from essentially planar to highly twisted. Depending on the oxidation state of the central metal ion of the complex, the ligand structure and the nature of the possible counterion, salen complexes have coordination geometries from 4-coordinate square planar to 8-coordinate dodecahedron with varying degree of distortion (Fig. 12).

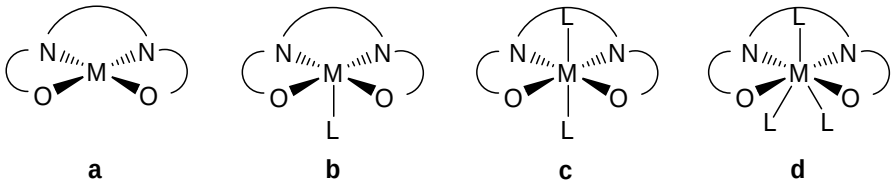


Fig. 12 The four most common coordination modes of the salen complexes, **a**= square planar, **b**= square pyramidal, **c**= octahedral and **d**= pentagonal bipyramidal coordination. L= charged or neutral ligand.

The coordination in monomeric complexes is different from that in oligomeric or polymeric ones. There are three very common coordination modes of salen complexes: 1) (distorted) square planar, usually observed in monomeric complexes with metal ion in oxidation state +2[72] and higher valent complexes with non-coordinating counterions, such as BF_4^- or PF_6^-;[73] 2) square pyramidal 5-coordinate mode, characteristic of complexes with coordinating counterions (halides,[74] oxygen- and carbon-based anions,[75, 76] nitrido[77]) and metal ions in oxidation state +3, and of complexes containing a non-charged neutral ligand (water,[78] alcohol,[79] pyridine[80]); 3) octahedral coordination (6-coordinate) mode, which is common for many complexes, independent of the oxidation state of the metal ion (examples include M^{6+} and M^{4+} complexes with two coordinating anions,[81, 82] and M^{3+} complexes with two neutral ligands[83]).

7-Coordinate complexes usually contain high-valent early transition metal ions, and often a coordinating neutral ligand such as THF ($Zr(salen)Cl_2 \cdot THF$[84]). Another common type of 7-coordinated salen complexes is dioxouranium complexes containing a coordinated solvent molecule.[85] 8-Coordinated salen complexes are rare; two examples of such compounds are $Er(salen)_2 \cdot (pipH)$,[86] where pipH= piperidinium (Fig. 13) and $Zr(salophen)_2 \cdot 2.5C_6H_6$.[87] The former complex consists of $[Er^{3+}\text{-}(salen)_2]^-$ anions and $(pipH)^+$ cations and has a distorted square antiprism coordination around the Er^{3+} ion. The latter complex has dodecahedral coordination with two $(salophen)^{2-}$ anions around a Zr^{4+} ion.

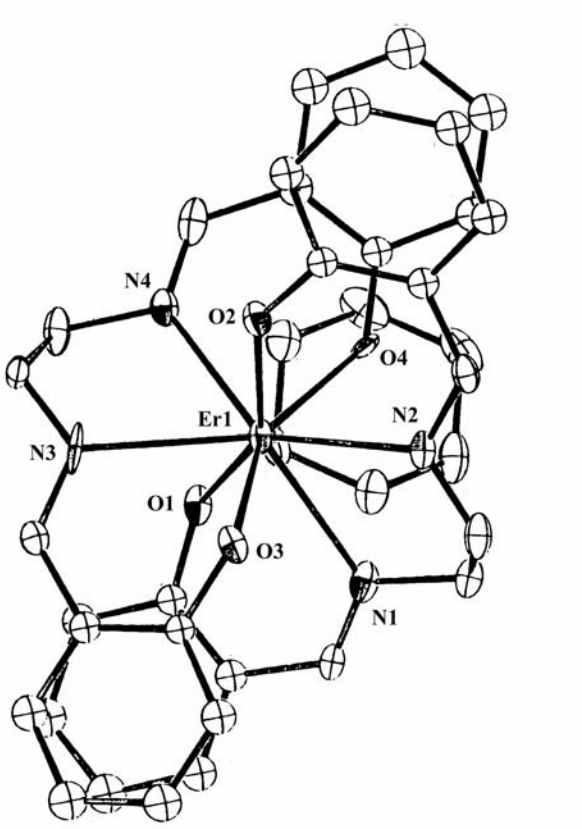
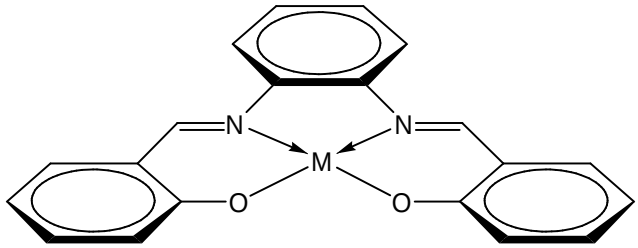


Fig. 13 Crystal structure of the 8-coordinated erbium complex. Counterion and hydrogen atoms are omitted for clarity. Reprinted from ref. 86, Copyright (1989), with permission from Elsevier.

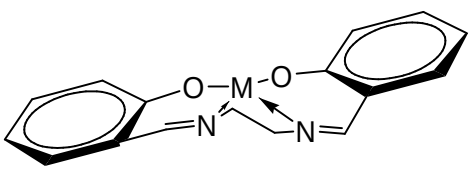
The coordination mode of the donor atoms of the salen ligand itself varies. Ligands in which the diamino moiety is constructed from 1,2-diaminoaromatics are forced to adopt planar geometry (Fig. 14).



27

Fig. 14 Planar metal-salophen structure.

Ligands with aliphatic (cyclic or acyclic) diamine moiety adopt more or less distorted planar geometry in metal complexes. Depending on the compound, this leads to stepped (**28**) or umbrella-like (**29**) conformations (Fig. 15). The stepped *trans*-folded structure is the most common coordination geometry in salen-type complexes, the umbrella-like conformation being much rarer.



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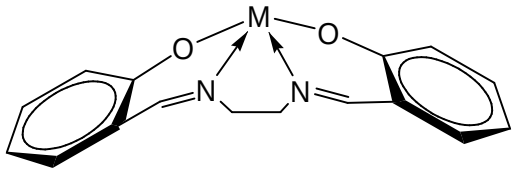

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Fig. 15 Stepped (**28**) and umbrella (**29**) conformations in salen-type complexes.

In some salen-type complexes the ligand adopts *cis*-folded structure (Fig. 16). This is the case in compounds where the diamine moiety is constructed from 2,2'-diaminobinaphthyl[88] and in some complexes of zirconium and hafnium.[19] If the salen ligand has substituents at the imine carbons, *cis*-

β-folded conformation is adopted to avoid steric repulsion.[27] Owing to the geometry, c*is*-folded complexes are chiral whether or not the free ligand is.[27] In particular, *cis*-β-folded complexes have interesting catalytic applications.

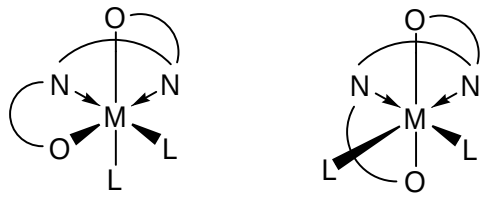


Fig. 16 Schematic drawing of **a**=*cis*-β- and **b**=*cis*-α-folded conformations. L=charged or neutral ligand or vacant site.

The conformation of the salen complex in solid state can be unambiguosly solved by X-ray crystallography. NMR spectrometry can be applied for studies in solution. Planar and *trans*-folded complexes are usually C_2-symmetric, causing the imine protons to have identical chemical shifts. Complexes that are *cis*-folded are not C_2-symmetrical and their imine protons resonate at different frequencies.[27]

3. SALEN-CATALYSED OXIDATIONS

3.1. General description of metal-oxygen complexes

Many transition metal complexes form coordination compounds with oxygen. These complexes can be of superoxo, peroxo, oxo or hydroperoxo type (Fig. 17).[89-92] Upon formation of these complexes, the metal ion donates unpaired electrons to the oxygen and is thus oxidised, formally by one or two electrons. In reality, the electron transfer is not complete, and the metal ion has

properties between the lower and the higher oxidation state. This is especially true with reversible oxygen carriers.[93, 94]

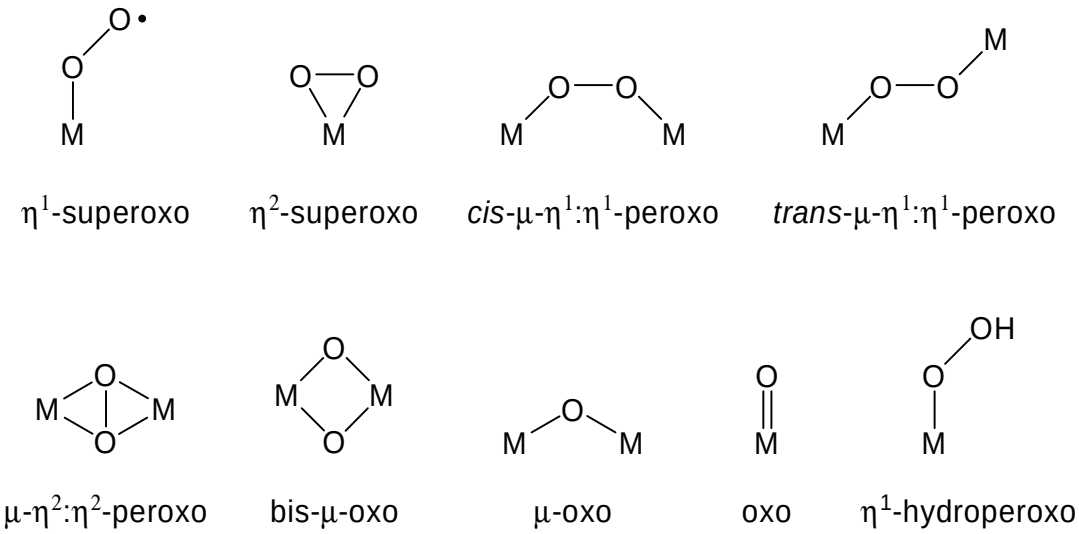


Fig. 17 Coordination modes of oxygen to the metal in transition metal complexes.

Superoxo and peroxo complexes are easily formed by reaction of triplet state dioxygen $^3O_2$ and a transition metal ion with unpaired electrons available to donate to the oxygen molecule. Upon complexation, the metal ion also receives and donates electron density (π-backbonding).[91] On the other hand, formation of the oxo complexes from molecular oxygen requires breaking of the O–O bond, which is achieved by reduction of the dioxygen with four electrons. Thus oxo complexes are mostly observed with metal ions such as manganese[74, 95] and iron[96, 97] that are capable of existing at several oxidation states. An easier way to prepare oxo complexes is with oxo transfer reagents and peroxides such as NaOCl, iodosylarenes, H_2O_2, organic hydroperoxides, peroxy acids and peroxysulfates that possess an easily heterolysed O–O bond.

Oxygen-oxygen and metal-oxygen bond lengths have been determined in various species. The O–O bond length in triplet state oxygen, $^3O_2$, is 1.207 Å,[98] while in hydrogen peroxide it is considerably longer, 1.49 Å.[99] In simple superoxide compounds, the distance lies between these two values (in KO_2 1.33 Å).[100]

Many superoxo complexes with η^1-coordination have been characterised by X-ray crystallography. The first crystallographically characterised Rh^{3+}-η^1-superoxo complex, which was synthesised by Bakac and Guzei (Fig. 18),[101] contains a tetraaza macrocyclic ligand to chelate rhodium ion. The O–O bond length is 1.306(5) Å.

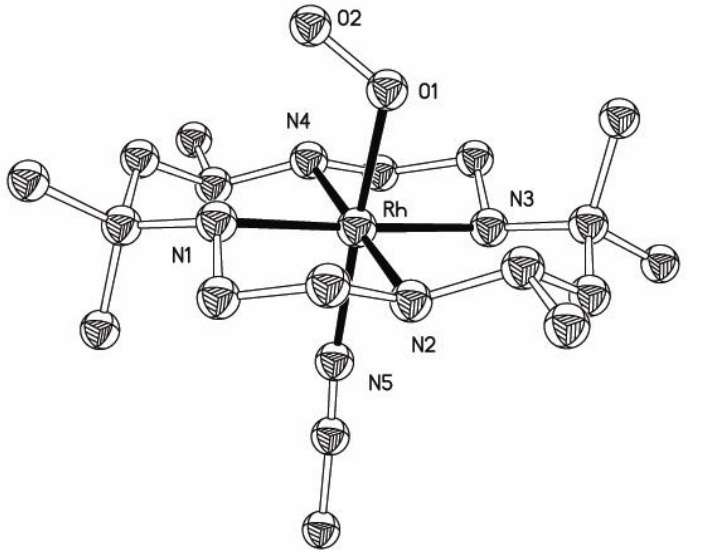


Fig. 18 Crystal structure of the Rh^{3+} complex with coordinated η^1-superoxo ligand. Counterions and hydrogen atoms are omitted for clarity. Selected bond lengths (Å): O1–O2 1.306(5); Rh–O1 2.005(3).[101]

The first structural characterisation of a Cu^{2+}-superoxo complex with η^1-coordination mode was published in 1994.[102] The tripodal ligand in this complex was tris[(6-pivaloylamino)-2-pyridyl)methyl]amine (Fig. 19). The bond length in the superoxo ligand is somewhat shorter than that in the rhodium complex, 1.235(9) Å, but it falls within the expected range for coordinated η^1-superoxo ligand.[103, 104]

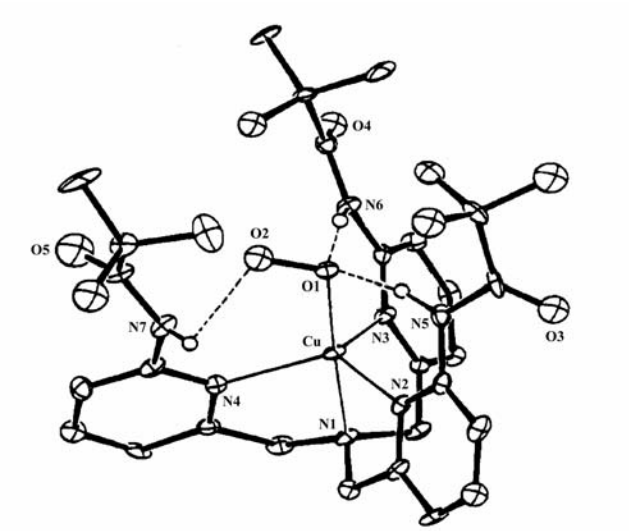


Fig. 19 Crystal structure of the tripodal Cu^{2+} complex with η^1-superoxo ligand. The counterion and most of the hydrogen atoms are omitted for clarity. Selected bond lengths (Å): O1–O2 1.235(9); Cu–O1 1.881(3). Reprinted with permission from ref. 102. Copyright (1994) American Chemical Society.

Although salen complexes with η^1-superoxo ligands have not been characterised recently, some earlier studies have been published. One example is shown in Fig. 20. In the crystals of this complex, the O–O bond length is 1.282(2) Å. The other apical position is occupied by aqua ligand.[105]

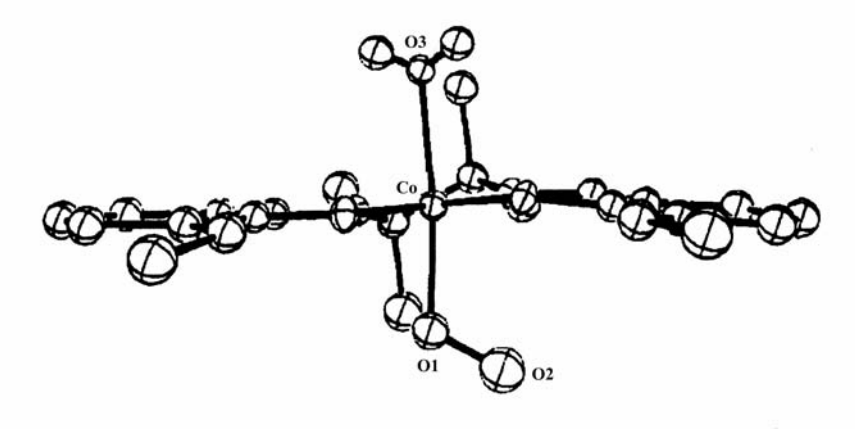


Fig. 20 Crystal structure of a salen-type cobalt complex with η^1-coordinated superoxo ligand. Hydrogen atoms, except the ones in aqua ligand, are omitted for clarity. Selected bond lengths (Å): O6–O7 1.282(2); Co–O6 1.868(2). Reprinted with permission from ref. 105. Copyright (1979) American Chemical Society.

Crystallographically characterised η^2-superoxo complexes are rare. To my knowledge, no salen-type complexes with η^2-superoxo ligands have been characterised by X-ray crystallography. A recent crystal structure determination of a Cr^{3+} complex with hydrotris(pyrazolyl)borato-type ligand containing a η^2-coordinated superoxo ligand (the first structurally characterised Cr^{3+} complex with η^2-superoxo ligand) revealed an O–O bond length of 1.327(5) Å (Fig. 21).[106] Cu^{2+} and Co^{2+} complexes with similar hydrotris(pyrazolyl)borato ligands have been characterised. The Cu^{2+} complex is the first structurally characterised η^2-superoxo complex with copper.[107] Here the superoxo bond length is 1.22 Å, while the Co^{2+} complex has a superoxo bond length of 1.262(8) Å.[108] The O–O bond lengths in these two complexes are typical of the η^2-superoxo ligand.[109]

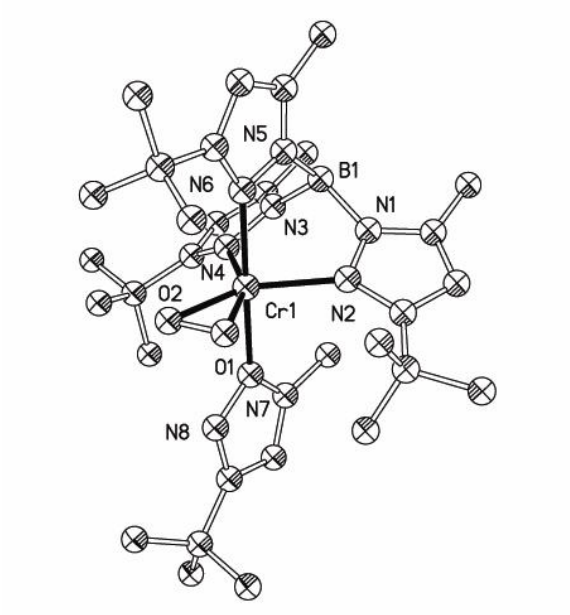


Fig. 21 Crystal structure of a Cr^{3+} complex with η^2-superoxo ligand. Counterion and hydrogen atoms are omitted for clarity. Selected bond lengths (Å): O1–O2 1.327(5); Cr1–O1 1.861(4); Cr1–O2 1.903(4).[106]

Co(salen) complex with a *cis*-μ-η^1:η^1-peroxo ligand was crystallised and characterised by X-ray crystallography in 1970.[110] This binuclear complex also contained two molecules of DMF coordinated to the second apical positions of the octahedral cobalt ions (Fig. 22). The O–O and Co–O bond lengths are 1.339(6) and 1.910(6) Å, respectively. The peroxo bond length is in the expected range for μ-peroxo cobalt complexes,[94] although the geometry of the complex was somewhat unusual for peroxo ligation.

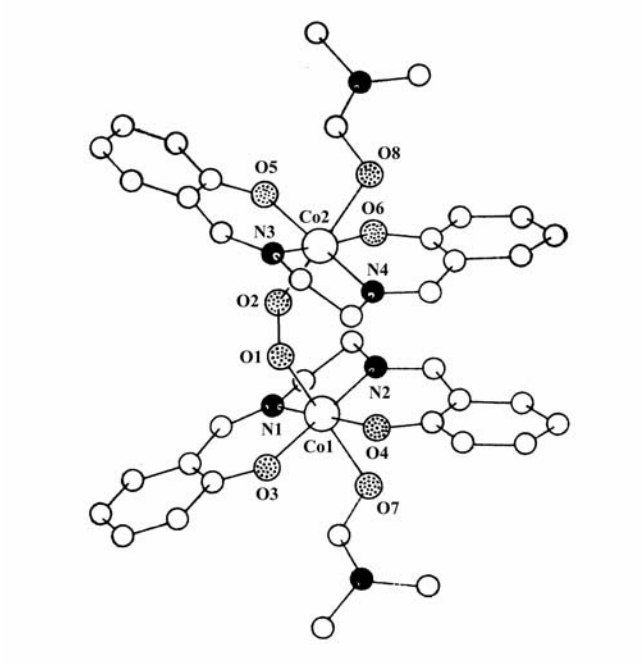


Fig. 22 Crystal structure of the binuclear Co(salen) complex with coordinated *cis*-μ-η^1:η^1-peroxo and DMF ligands. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): O1–O2 1.339(6); Co1–O1 1.910(6); Co2–O2 1.910(6).[110] Reproduced by permission of The Royal Society of Chemistry.

In the *cis*-μ-η^1:η^1-peroxo complex of binuclear Co^{3+} compound having bridging acetato, benzoato and phenolato ligands, the lengths of the O–O bonds are 1.422(3) Å (acetato bridge) (Fig. 23) and 1.43(2) (benzoato bridge).[111] The O–O bond lengths in μ-peroxo Co^{3+} complexes are sometimes unusually short, ranging from 1.308 to 1.488 Å.[94]

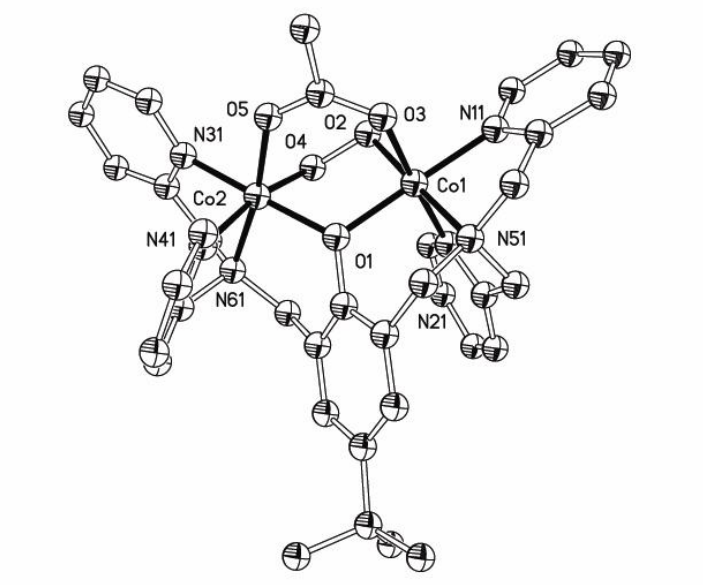


Fig. 23 Crystal structure of the binuclear Co^{3+} complex having a *cis*-μ-η^1:η^1-peroxo ligand. Counterions and hydrogen atoms are omitted for clarity. Selected bond length (Å): O2–O4 1.422(3); Co1–O2 1.875(2); Co2–O4 1.873(2).[111]

The crystal structure of binuclear Co(salen) with *trans*-μ-η^1:η^1-peroxo and piperidine ligands coordinated to cobalt ions has been determined by Avdeef and Schaefer.[112] The sixth coordination positions of the cobalt ions are occupied by piperidine ligands giving octahedral coordination around cobalt (Fig. 24).

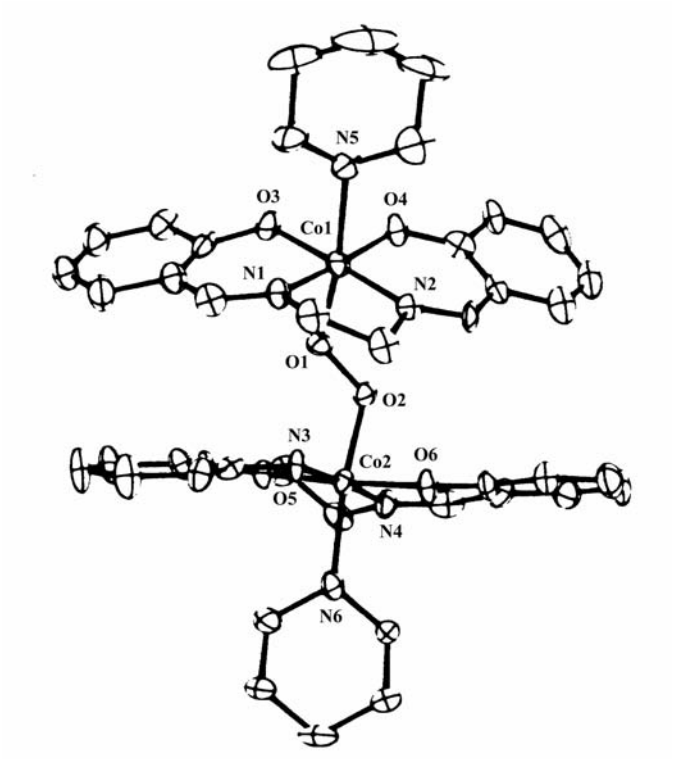


Fig. 24 Crystal structure of the binuclear Co(salen) with *trans*-μ-η^1:η^1-peroxo- and piperidine ligands. Solvate molecule and hydrogen atoms are omitted for clarity. Selected bond lengths (Å): O1–O2 1.383(7); average Co(1,2)–O(1,2) 1.911(4). Reprinted with permission from ref. 112. Copyright (1976) American Chemical Society.

The crystal structure of the binuclear *trans*-μ-η^1:η^1-peroxo Cu^{2+} complex having tripodal tris(*N*-benzylaminoethyl)amine ligands was recently determined.[113] In this complex the O–O bond distance is 1.450(5) Å, slightly shorter than in H_2O_2.

The O–O bond length in μ-η^2:η^2-type peroxo complexes is usually about the same as in hydrogen peroxide. For example, in the binuclear Cu^{2+} complex shown in Fig. 25, the O–O bonds are 1.491(5) and 1.487(5) Å (not shown).[114] In a crystallographically characterised Mn^{4+} porphyrin

bond length in peroxo ligands is close to or somewhat shorter than that observed for hydrogen peroxide itself, the extreme values being 1.30 and 1.62 Å.[103, 116, 117]

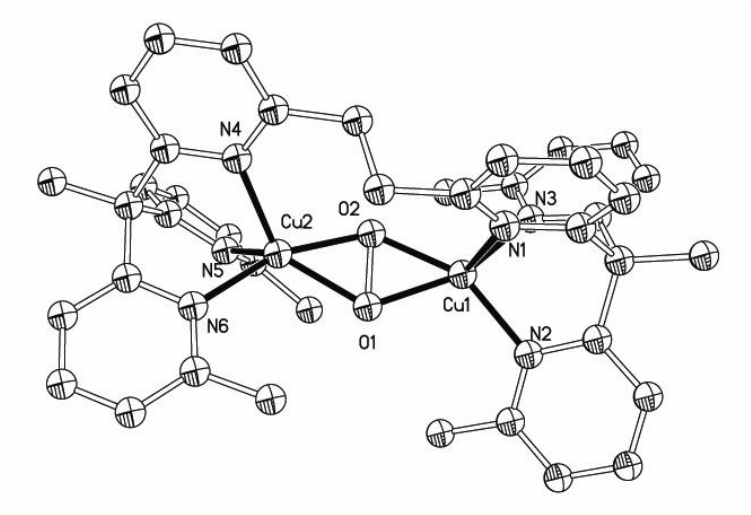


Fig. 25 Crystal structure of the μ-η^2:η^2-peroxocopper complex. Counterions and hydrogen atoms are omitted for clarity. Selected bond lengths (Å): O1–O2 1.491(5); Cu1–O1 1.918(4); Cu1–O2 1.913(3); Cu2–O1 1.961(4); Cu2–O2 1.894(4).[114]

Of the complexes containing a η^1-hydroperoxo ligand, a palladium compound with hydrotris(3,5-diisopropylpyrazolyl)borato ligand has been synthesised and characterised by Akita *et al.* (Fig. 26).[118] The O–O bond length in the hydrogen-bonded hydroperoxo ligand was found to be 1.463(9) Å.

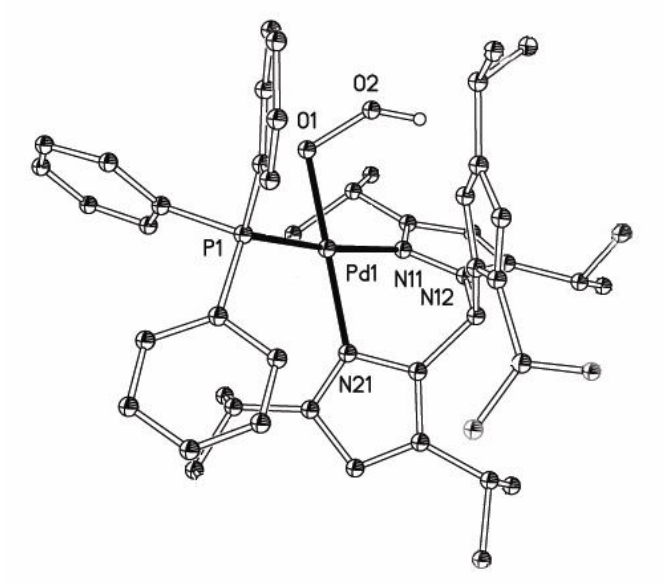


Fig. 26 Crystal structure of the Pd^{+} complex containing a η^1-coordinated hydroperoxo ligand. Solvate molecules and hydrogen atoms, expect the one in hydroperoxo ligand, are omitted for clarity. Selected bond lengths (Å): O1–O2 1.463(9); Pd1–O1 1.981(7).[118]

Co^{3+} complex with *meso*-5,7,7,12,14,14-Me_6-[14]aneN_4 ligand and an additional coordinated η^1-hydroperoxo ligand was prepared and characterised by X-ray crystallography by Guzei and Bakac.[119] The geometry around cobalt in this first structurally characterised Co^{3+}-hydroperoxo complex is slightly distorted octahedral, with the hydroperoxo and acetonitrile ligands occupying apical positions (Fig. 27). The bond length in the hydroperoxo ligand was found to be 1.397(4) Å. The bond lengths in the two above hydroperoxo complexes are typical.[94, 103]

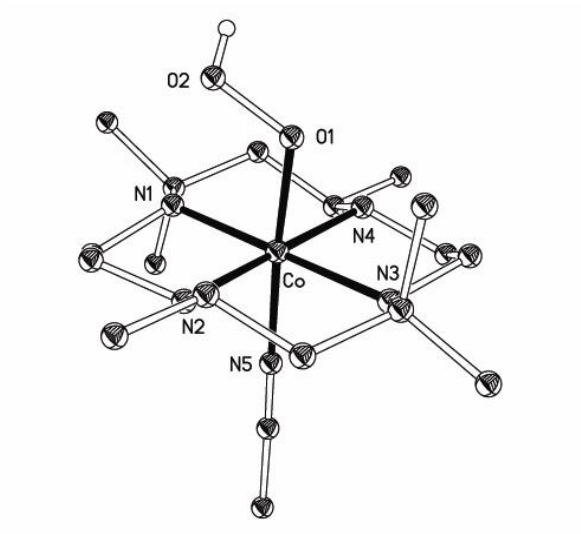
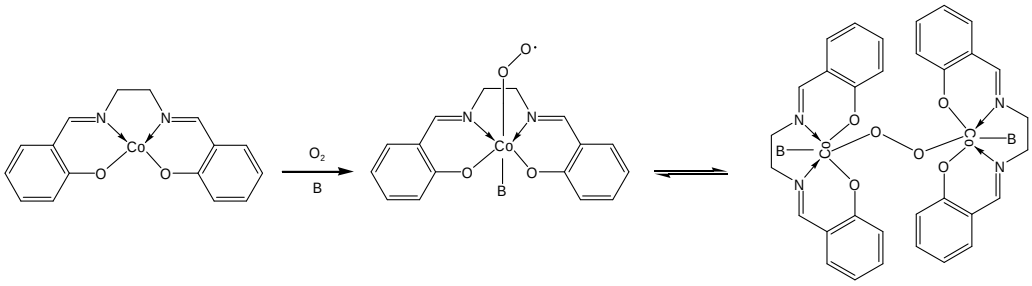


Fig. 27 Crystal structure of the Co^{3+} complex with η^1-hydroperoxo ligand. Counterions and hydrogen atoms, except the one in the hydroperoxo ligand, are omitted for clarity. Selected bond lengths (Å): O1–O2 1.397(4); Co–O1 1.878(3).[119]

Metal-oxygen bond length in the complex types shown in Fig. 17 is dependent on the metal ion and the mode of the oxygen coordination. Some typical values are shown in Figs. 18-27. The observed range is from < 1.55 Å to > 2.23 Å, the most typical length for first-row transition metal superoxo, peroxo and hydroperoxo complexes being about 1.8-1.9 Å.[94, 109] In μ-oxo and bis-μ-oxo binuclear complexes, the M–O bond length is usually close to 1.8 Å. Terminal metal-oxo complexes have a range of shorter M–O bonds, ranging from < 1.55 Å[120, 121] to > 1.81 Å[122] in some rare cases.

Cobalt is one of the most investigated metals in the complexes of salen-type ligands formed from dioxygen. As long ago as 1938, Tsumaki[123] found that the simple complex Co(salen) **33** changed colour when exposed to air and concluded that it can bind dioxygen reversibly. This finding provided the basis for an intensive and ongoing interest in the oxygen-carrying cobalt complexes.

Later studies have revealed that the oxygen binding ability and the catalytic activity of the cobalt complexes can be increased through the addition of base (such as pyridine).[124, 125] Some Co(salen)-O_2-base adducts are stable enough for their crystal structure to be determined (*vide infra*). (For more examples, see ref. 126.) The X-ray structures confirmed that Co(salen)-type complexes form oxygen adducts of mononuclear superoxo (**34**) and binuclear peroxo type (**35**), depending on the structure of the ligand and reaction conditions (Scheme 4). At room temperature, the binuclear peroxo complex is favoured.[90]



33 34 35

Scheme 4 Formation of Co(salen)-(η^1-superoxo)- and Co(salen)-(μ-η^1:η^1-peroxo) complexes. B=base.

Superoxo and peroxo complexes are also common with iron, although iron-salen complexes more often form oxo-type compounds. Sterically hindered "picket-fence" porphyrins, in which one side of the porphyrin macrocycle (coordination site of the oxygen) is protected by large substituents, form superoxo complexes similar to oxyhaemoglobin.[127] These complexes are of great interest as models for haemoglobin and cytochromes.[128]

A manganese complex $[Mn(TPP)O_2]^-\cdot[K(K222)]^+$ (K222=4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]-hexacosane) containing a peroxo ligand was characterised by X-ray crystallography in 1987 (Fig. 28).[115] The peroxo ligand is η^2-coordinated. Mössbauer, EPR and

magnetic susceptibility data for an analogous iron complex $[Fe(OEP)O_2]^-\cdot[Me_4N]^+$ are consistent with a similar geometry.[129] In these porphyrin complexes the peroxo ligand is not derived from dioxygen; instead KO_2 was used to deliver the O_2^--ligand.

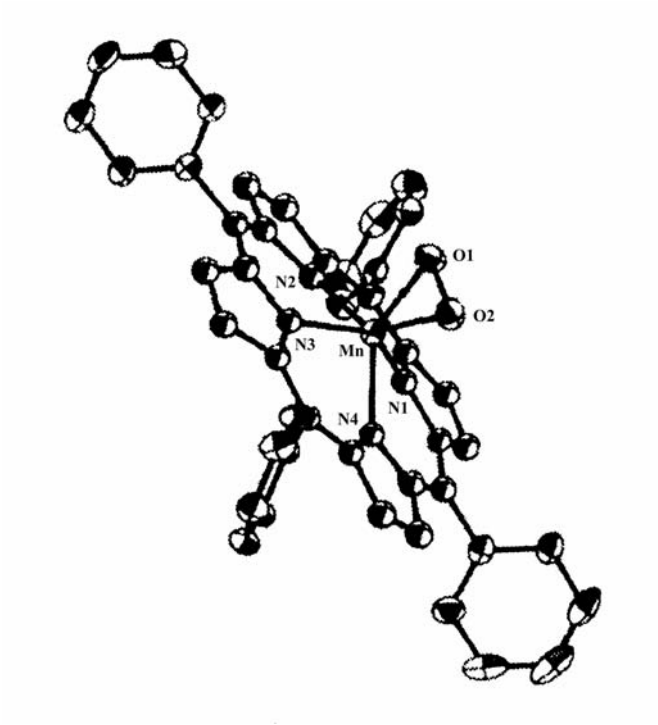


Fig. 28 Crystal structure of the $[Mn(TPP)O_2]^-\cdot[K(K222)]^+$. Counterion and hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Mn–O1 1.901(4); Mn–O2 1.888(4); O1–O2 1.421(5). Reprinted with permission from ref. 115. Copyright (1987) American Chemical Society.

Mn(salen) complex **5** also forms transient superoxo or peroxo complex with dioxygen in ionic liquid $[bmim]^+[PF_6]^-$, although this reaction requires electrochemical reduction of **5** to a corresponding Mn^{2+} complex before dioxygen can coordinate.[130] Mukaiyama and co-workers[131-134] have extensively studied aerobic epoxidation of olefins using manganese complexes as catalysts and

aldehydes as sacrificial coreductants. They found both salen[131] and β-ketoiminato[132-134] complexes to be efficient catalysts and presumably to form active acylperoxo compounds with dioxygen and aldehyde.

Many other transition metal compounds with a myriad of ligands also form superoxo, peroxo and hydroperoxo complexes. Coordination modes of oxygen in these complexes are those shown in Fig. 17.[90, 135] In conclusion, the nature of the coordinated superoxo, peroxo or hydroperoxo ligand can be deduced from the O–O bond length. In superoxo complexes this bond is usually a little over 1.2 Å long, whereas in peroxo and hydroperoxo complexes it is ±1.4 Å.

Salen-type oxo complexes are well known and numerous examples exist. Common metals in these kinds of complexes are titanium, vanadium, chromium, manganese, iron and molybdenum. Titanium often forms binuclear bis-μ-oxo-type[136] or mononuclear μ-oxo-type complexes,[137] where the vanadium,[138, 139] chromium,[140-142] manganese[143-145] and molybdenum[146-148] favour mononuclear terminal oxo-type coordination. μ-Oxo coordination mode is common in iron complexes (Fig. 29).[149-151]

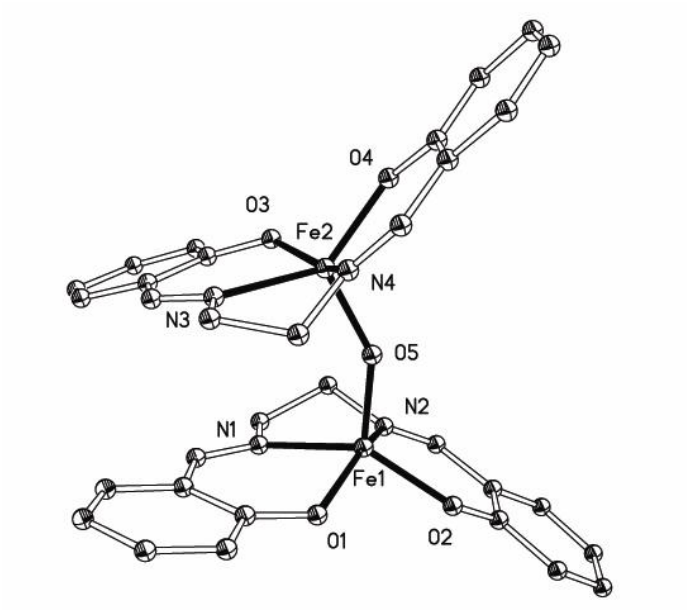


Fig. 29 Crystal structure of the μ-oxo complex [{Fe(salen)}$_2$O]. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Fe1–O5 1.781(1); Fe2–O5 1.786(1).[151]

Similar bridged binuclear complexes of Mn^{4+} with bis-μ-oxo ligands have been reported.[152, 153] The crystal structure of one of these complexes, [Mn(salbn)(μ-O)]$_2$, is shown in Fig. 30.

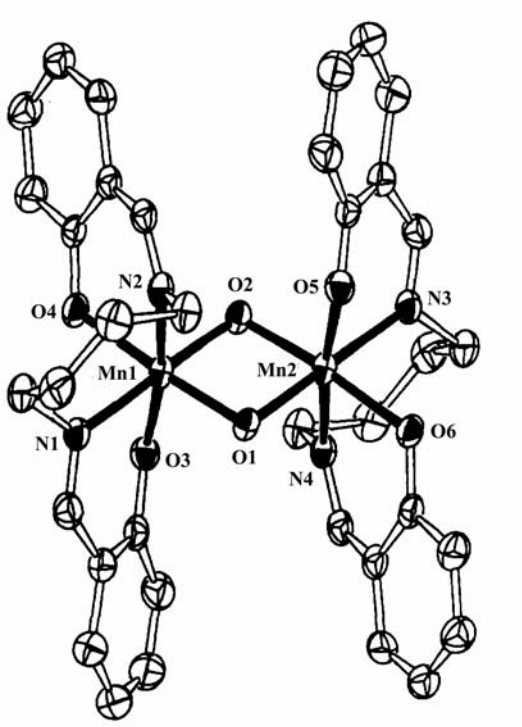


Fig. 30 Crystal structure of the complex $[Mn(salbn)(\mu\text{-}O)]_2$. Solvate molecules and hydrogen atoms are omitted for clarity. Selected bond lengths (Å): Mn1–O1 1.819(2); Mn1–O2 1.826(2). Reprinted from ref. 153, Copyright (1998), with permission from Elsevier.

Salen-type non-bridged terminal oxo complexes of vanadium, chromium and molybdenum tend to be stable compounds, and many of them have been crystallographically characterised (Fig. 31). Despite its short Cr–O bond, the complex shown in Fig. 31 was able to transfer oxygen atom to alkenes. Crystal structures of oxochromium-salen complexes with additional donor ligands have also been determined.[140-142]

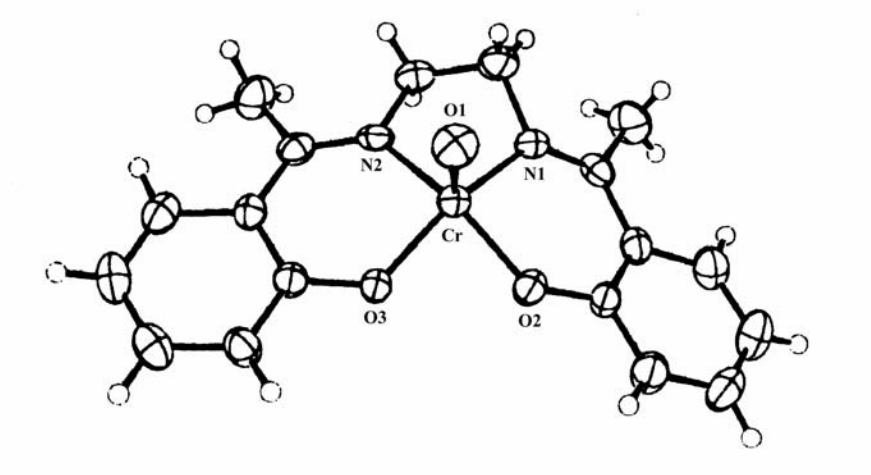


Fig. 31 Crystal structure of the stable terminal oxo complex of Cr^{5+} with substituted salen ligand. The counterion is omitted for clarity. Selected bond length (Å): Cr–O1 1.545. Reprinted with permission from ref. 140. Copyright (1985) American Chemical Society.

In contranst, salen-type Mn^{5+}-oxo complexes are highly reactive and they have only been characterised by spectrometric methods.[143, 145, 154] Formation of a salen-Mn^{5+}-oxo complex through the reaction of Mn^{3+}-salen precursor complex with iodosylbenzene in acetonitrile was confirmed by ESI tandem mass spectrometry (Fig. 32). The high intensity peak at *m/z* 548.8 shown in Fig. 32 corresponds to a doubly charged iodosylbenzene complex with binuclear μ-oxo compound.

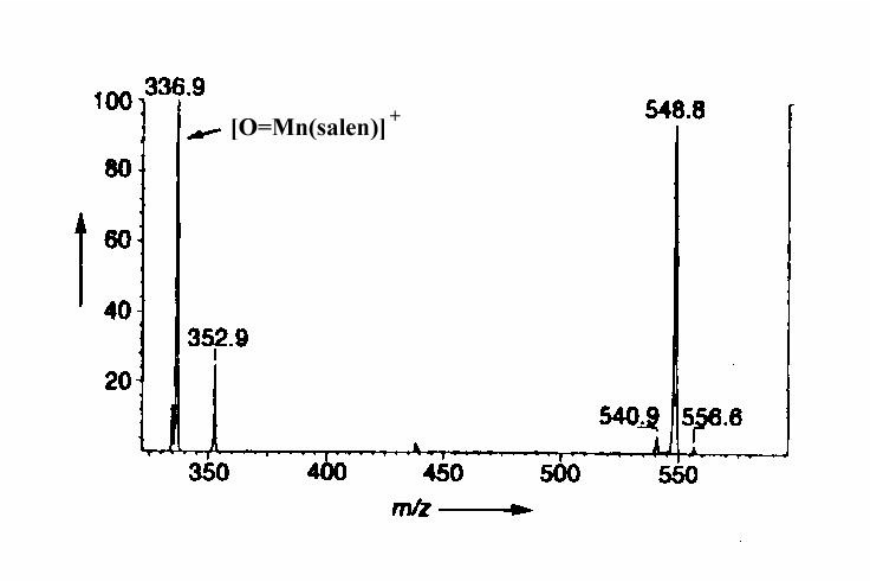


Fig. 32 ESI mass spectrum showing the prominent peak of oxomanganese salen cation at *m/z* 336.9. Reprinted with permission from ref. 143, Copyright (1997) Wiley-VCH Verlag GmbH.

Stable Mn^{5+}-oxo complexes with tetraamido-type ligands have been synthesised and crystallographically characterised by Collins and co-workers[120, 121] (Fig. 33). The Mn–O triple bonds in these complexes are unusually short and strong, the Mn–O distances being just 1.548 and 1.549 Å. Because of the very strong Mn–O bond, and the cooperative effect of the alkali metal coordination to the pyridine nitrogen N5, only the complex shown in Fig. 33 was effective in oxygen atom transfer. This terminal oxo complex was synthesised from the corresponding Mn^{3+} complex in acetone using *tert*-butyl-hydroperoxide as oxidant. With a similar complex containing no pyridine nitrogen, oxygen atom transfer was not observed because of the strong Mn–O bond.

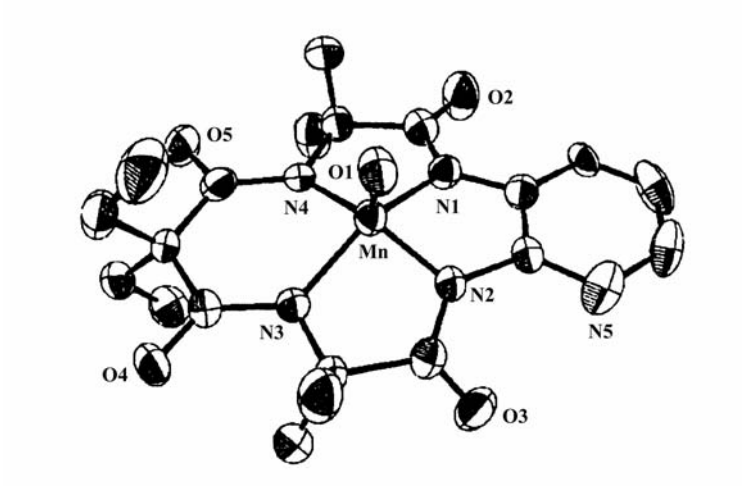


Fig. 33 Crystal structure of the stable Mn^{5+}-oxo complex with tetraamido ligand. Counterion and hydrogen atoms are omitted for clarity. Selected bond length (Å): Mn–O1 1.549(3). Reprinted with permission from ref. 121. Copyright (1998) American Chemical Society.

A slightly longer terminal metal-oxo bond was observed in the nonheme Fe^{4+}-oxo complex with 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane (TMC) ligand.[155] The corresponding Fe^{2+} complex $[Fe(TMC)(OTf)_2]$ reacted with H_2O_2 in acetonitrile to yield the solvated complex $[Fe(O)(TMC)(MeCN)](OTf)_2$. The Fe–O double bond length is 1.646(3) Å, which is a value between the single M–O bond lengths shown in Figs. 18-30 and the multiple M–O bond lengths shown in Figs. 31 and 33.

3.2. Metallosalen complexes as oxidation catalysts

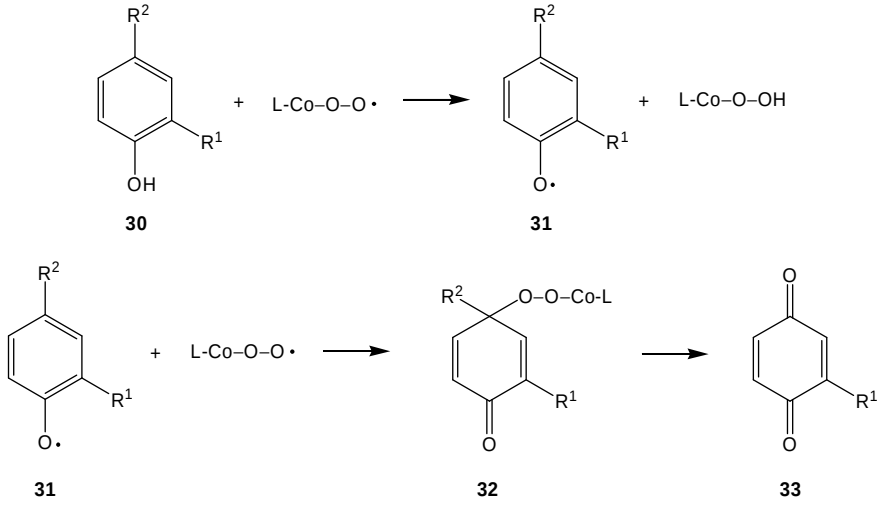
Salen-type transition metal complexes have been used as catalysts for a very wide range of oxidative transformations of organic compounds. This area of research is so vast that it is impossible to cover it all here. In the following discussion, I will concentrate on the catalytic

oxidation of phenolics, benzylic alcohols and lignin-like materials with salen-type complexs of chromium, manganese, iron, cobalt and copper.

3.2.1. Oxidation of phenolic materials

Perhaps the oldest and one of the most widely studied combinations of the substrates and metals mentioned in section **3.2.** is phenolic material and cobalt. The first example of the use of Co(salen) to catalyse phenol oxidation with dioxygen was published in 1967.[156] The oxidations of phenolics using Co(salen)-type catalysts have mostly been performed in organic solvents.

In Co(salen)-type complexes, the state of the coordinated oxygen species influences the reactivity of the complex. With dioxygen as oxidant, in normal conditions (room temperature, ambient oxygen pressure, nonpolar solvent), the less reactive binuclear, bridged peroxo complex is favoured in the equilibrium solution of Co(salen)-oxygen adducts, but the equilibrium can be shifted towards the more catalytically active mononuclear superoxo complex by tuning the reaction conditions.[90] Co(salen)-superoxo complexes, where the dioxygen is reduced by one electron, behave much like radicals in oxidation reactions. This is the generally accepted mode in the oxidation of phenolic substrates.[125, 157] The mechanism of the oxidation reaction has been postulated as follows: a radical superoxo complex abstracts the phenolic hydrogen atom to produce phenoxy radical, which is then reacted with another superoxo complex or dioxygen, leading to 1,4-benzoquinone (**33**) products (Scheme 5).[158]

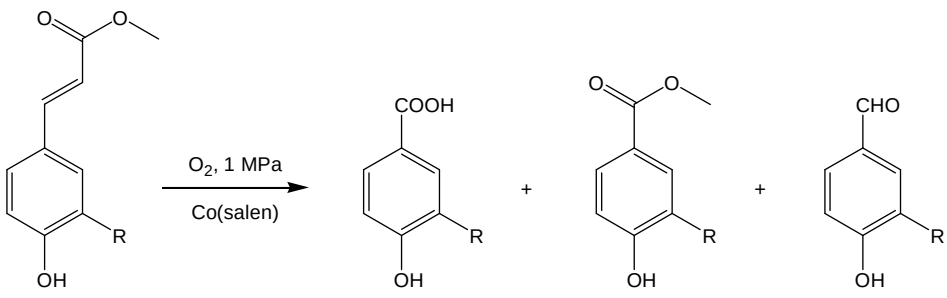


Scheme 5 Postulated mechanism of phenol oxidation reactions with dioxygen catalysed by Co(salen) and related complexes.[158]

Bozell and co-workers[125, 158] oxidised various *para*-substituted phenolics with dioxygen using Co(salen) and its derivatives as catalysts. The substituent at the *para*-position to the phenolic OH was cleaved off, yielding 1,4-benzoquinones as products. The 5-coordinated complexes Co(*N*-Me-salpr) and a pyridine adduct of Co(salen) were found to be much more reactive catalysts than the 4-coordinated Co(salen).[125, 158] When the substrate contained a benzylic OH-group, the corresponding carbonyl compounds were generally obtained in only low yield, if at all. These oxidations were carried out with oxygen pressure of 345 kPa.

A similar reaction, yielding 1,4-benzoquinone derivative from the phenolic benzyl alcohol derivative 1-(4-hydroxy-3-methoxyphenyl)-ethanol when oxidized with dioxygen and Co(salen) catalyst, was recently observed by Canevali *et al.*[159] The C–C bond cleavage in Co(salen)-catalysed oxidation of phenolic methyl cinnamates was observed by the same group. In these cases the double bond of the cinnamate side chain was cleaved, yielding benzoic acids, methyl benzoates and

benzaldehydes as oxidation products (Scheme 6). If the substituent R in the substrate was chlorine, no oxidation was observed.[160, 161] Mechanistic studies based on EPR spectrometry supported the superoxo-mediated radical mechanism in these reactions. Oxygen pressure of 1 MPa was applied.



34 R=OMe
35 R=H

36 R=OMe
37 R=H

38 R=OMe
39 R=H

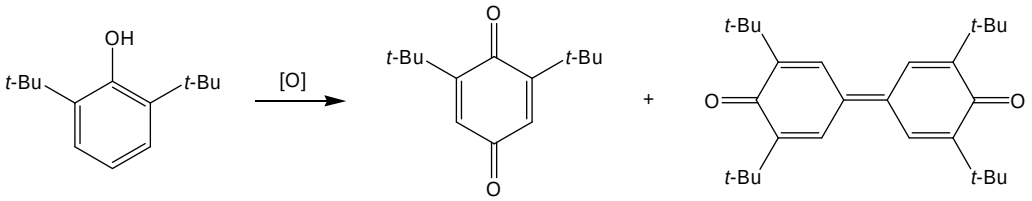
40 R=OMe
41 R=H

Scheme 6 Oxidation of phenolic methyl cinnamates with dioxygen catalysed by Co(salen).[160, 161]

The structure of the substrate has a crucial effect on the outcome of the reaction, as is seen from the reactions above, and sometimes more exotic products are obtained, such as 1,5-cyclohexadienone derivatives.[162, 163] Catechol derivatives, such as 3,5-di-*tert*-butylcatechol, often give the corresponding 1,2-benzoquinones as products, with good selectivities.[164, 165]

One of the most widely studied phenolic substrates in catalytic oxidations is 2,6-di-*tert*-butylphenol **42**, because the only oxidation products are 2,6-di-*tert*-butyl-1,4-benzoquinone **43** and 3,3',5,5'-tetra-*tert*-butyldiphenoquinone **44**. Analysis of the reaction outcome is thus facilitated (Scheme 7). With **42** as substrate, using several different Co(salen) derivatives as catalysts, Pui *et al.*[166] recently obtained very good yields and selectivities up to100% for **43**. The same substrate (**42**) has also been oxidised with dioxygen in supercritical CO_2 catalysed by the Co^{2+} analogue of **5**.[167] Benzoquinone **43** was obtained in good yields and selectivities. Curiously, under identical

conditions, 3,5-di-*tert*-butylphenol yielded only trace amounts of oxidation products. Again a radical mechanism was postulated, involving superoxo complex. An earlier publication, from 1984 describes the oxidation of **42**, along with phenolics such as 1-naphthol and its derivatives, with dioxygen, catalysed by different Co(salen) derivatives.[168] Products **43** and **44** were obtained, along with 1,5-cyclohexadienone derivatives. 1-Naphthols gave the corresponding 1,4-benzoquinones. Other catalyst types were used as well, namely dimethylglyoxime and porphyrin complexes. The role of the peroxy intermediates was discussed.



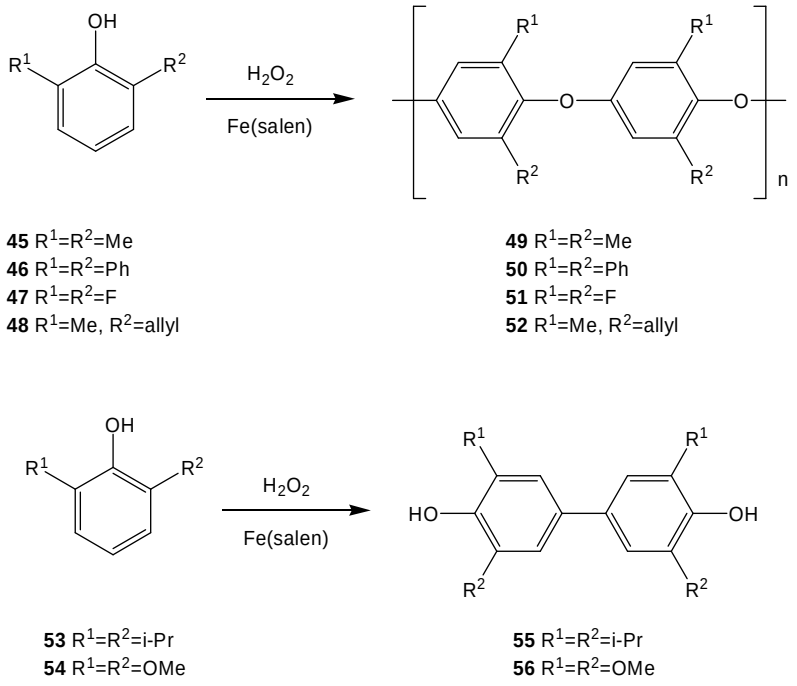
42 **43** **44**

Scheme 7 Oxidation of 2,6-di-*tert*-butylphenol **42** to corresponding benzoquinone **43** and diphenoquinone **44**.

Sippola *et al.*[169] have studied the oxidation of phenolic materials using Co(sulfosalen) (cobalt analogue of **10**) as catalyst and ambient pressure dioxygen as terminal oxidant in aqueous alkaline media. Almost 100% conversion to a C–C coupled biphenyl compound was achieved, when 4-methyl-2-methoxyphenol was used as substrate. The effect of the axial ligand was investigated, as were the kinetics of the reaction and the stability of the salen-type catalyst. It was found that the Co(sulfosalen) complex degrades in considerable degree under the conditions used. A mechanism involving hydrogen atom abstraction by the superoxo complex was suggested. The same group developed a method to follow the formation of the biphenyl product in the catalytic oxidation of 4-ethyl-2-methoxyphenol under similar conditions.[170]

Besides molecular oxygen, other useful terminal oxidants in the Co(salen)-catalysed oxidations of phenolics are *tert*-butylhydroperoxide and H_2O_2. Nishinaga *et al.*[171] have done an extensive study on the oxidation of *tert*-butylphenols with unsaturated side chains. A very wide range of products were obtained varying with the structure of the substrate. Usually the product contained a *tert*-butylperoxide substituent either in the aromatic ring or in the side chain. The mechanisms of the oxidations were postulated to proceed through hydrogen atom abstraction from the phenolic OH by *tert*-butylperoxo radical formed in the decomposition of the initial Co(salen)(OO-*t*-Bu) complex. Oxidation of phenol using H_2O_2 and Co(salen) yielded catechol and hydroquinone.[172] The postulated reaction mechanism involves a metal-hydroperoxo complex. Kinetics of the oxidation reaction was thoroughly investigated, and also with Cu(salen) and an analogue.

Fe(salen)-type complexes have successfully been employed as catalysts in the oxidative coupling of phenolics with H_2O_2 used as terminal oxidant. Kobayashi's group[173] have extensively studied the Fe(salen)-catalysed oxidative coupling of 2,6-disubstituted phenols. In the cases of 2,6-dimethyl-, 2,6-diphenyl- and 2-allyl-6-methylphenols, regular 1,4-phenyleneoxide polymers with MW about 10^4 were obtained, but 2,6-diisopropyl- and 2,6-dimethoxyphenol yielded C–C coupled biphenyl dimers (Scheme 8). The authors found that the formation of the diphenoquinone by-product is suppressed by the addition of a small amount of pyridine to the reaction mixture. Polymerisation of 2,6-difluorophenol using 1 mol-% of Fe(salen) and 1 eq. of H_2O_2 gave a good yield of crystalline poly(2,6-difluoro-1,4-phenyleneoxide) (Scheme 8) of very regular structure, in contrast to the enzymatic oxidation, which yielded irregular polymer resulting from the cleavage of fluorine atoms. Molecular weights up to 4400 were observed.[174]



Scheme 8 Oxidative coupling of 2,6-disubstituted phenols catalysed by Fe(salen).

Using a similar procedure, the Kobayashi group obtained poly(*m*-cresol) with MW > 10^6 by oxidation of enzymatically produced lower MW poly(*m*-cresol). They also extended their oxidative coupling method to produce poly(amino acid)-polyphenol hybrids and artificial wood polymers. Polyamino acids containing phenolic groups were polymerised with polyphenols to give ultra-high MW hybrid polymers with MW up to 1.67×10^6.[176] Again with the Fe(salen)-H_2O_2 system, cellulose derivatives with MW > 10^6 were obtained from cellulose derivatised with phenolic residues and poly(bisphenol-A), poly(*m*-cresol) or poly(*p-tert*-butylphenol).[177]

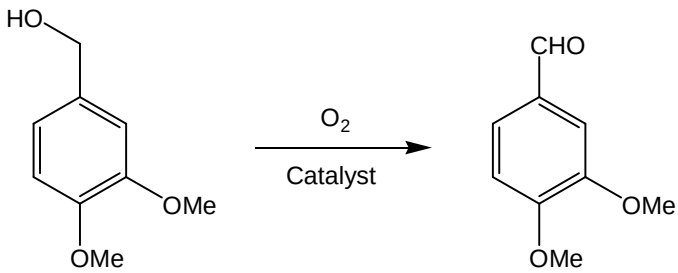
Study has also been made of the oxidative polymerisation of bisphenol-A, *m*-cresol, *p-tert*-butylphenol and phenol using hydrogen peroxide as terminal oxidant and binuclear [{Fe(salen)}$_2$(O)] (see Fig. 29 for crystal structure).[178] In this case the binuclear complex showed

even greater activity, requiring only 0.1 mol-% with respect to the monomer to give good yields of poly(bisphenol-A) with MWs of 1800-3400. Pyridine also had a beneficial effect on the polymer yield.

3.2.2. Oxidation of benzylic alcohols

The last few years have seen the appearance of a large number of papers describing the oxidation of benzylic alcohols catalysed by metallosalen complexes. A few examples of the oxidation of phenolic benzyl alcohols were given in the section **3.2.1**, and the reader is referred to refs. 125 and 159.

Oxidations of 3,4-dimethoxybenzyl alcohol **57** to 3,4-dimethoxybenzaldehyde **58** in aqueous alkaline media using Co(salen) and its derivatives as catalysts and dioxygen as terminal oxidant have been thoroughly investigated by Repo and co-workers (Scheme 9).[179-181]



57 **58**

Scheme 9 Oxidation of 3,4-dimethoxybenzyl alcohol to 3,4-dimethoxybenzaldehyde.

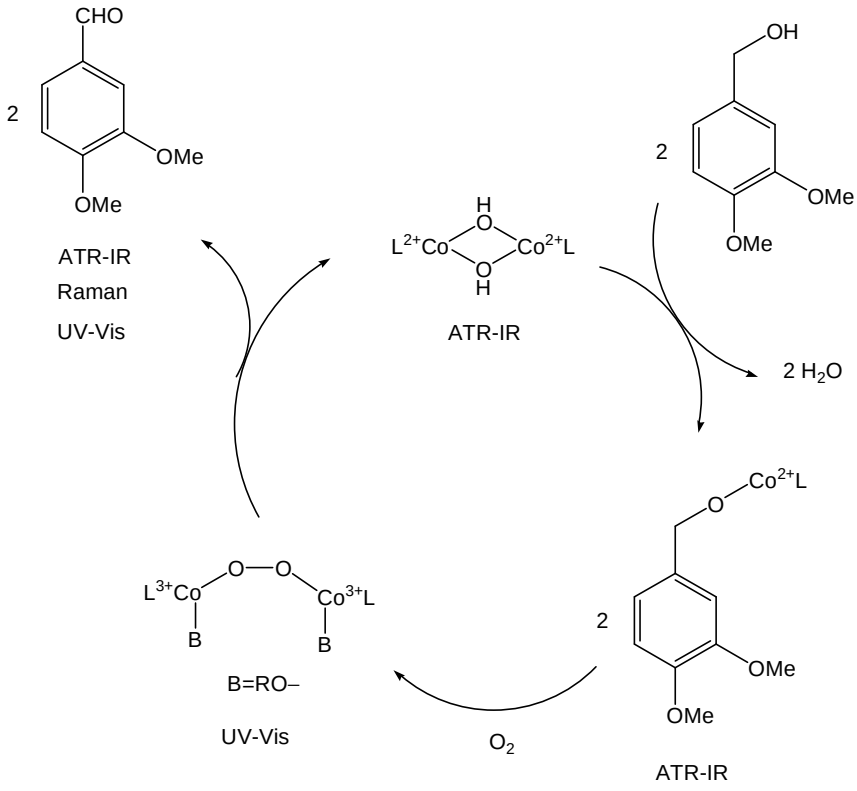
In the first of their studies they investigated the effect of reaction conditions on the outcome of the oxidation. It was found that an axially coordinating base is needed for the catalytic activity of 4-coordinated Co(salen) derivatives. Pyridine and diethylamine were efficient axial bases, while

ethylenediamine and imidazole appeared to inhibit the oxidation. The 5-coordinated complex Co(*N*-Me-salprn), with itramolecularly coordinating nitrogen atom, was found to be an inferior catalyst, as suggested by the rigidity of the axially coordinating nitrogen. The best temperature range for oxidations was 80–90 ºC, whereas below 60 ºC the oxidation did not proceed. A high pH was found to be necessary for good reactivity, the optimum pH value being 12.5. Conversion of the substrate ranged from 8 to 100%, depending on the catalyst and temperature. Turnover numbers (TONs) up to 28 were obtained with catalyst Co(salen). Atmospheric dioxygen pressure was used in all experiments.[179]

In their second publication,[180] the group investigated the effect of dioxygen pressure. The reactivity of the Co(salen) catalyst was found to increase linearly with dioxygen pressure. At 1 MPa, a TON of 103 was achieved. Examination was also made of the effect of the catalyst-substrate ratio. When the ratio dropped to 1:5950, a TON as high as 330 was obtained at ambient dioxygen pressure. Results were also good when NaOH or KOH was used to adjust the pH of the reaction medium. LiOH and $Ca(OH)_2$ gave much poorer results. Reactions proceeded selectively, yielding only 3,4-dimethoxybenzaldehyde as product, with no sign of the corresponding carboxylic acid in ^{1}H NMR spectra. There was no need for an additional axial base at high pH as OH^- evidently acted as one. The concentration of OH^- needed to be kept at a sufficient level; otherwise the reaction stopped because of the consumption of the OH^--ion in the reaction.

In the third study by the Repo group,[181] the reaction mechanism of the oxidation in aqueous alkaline media was investigated by *in situ* ATR-IR spectrometry. It was suggested that the mechanism involves the initial formation of a superoxo complex, which performs a two-electron oxidation of the substrate. Simultaneously, dioxygen is reduced to H_2O_2 and the Co(salen)(OH) complex is regenerated.[181]

A more detailed reaction mechanism was postulated later.[182] The oxidation reaction was monitored by multiple spectrometric methods and the mechanism shown in Scheme 10 was proposed.



Scheme 10 Revised reaction mechanism for the oxidation of 3,4-dimethoxybenzyl alcohol. L=salen ligand. Analytical methods for the detection of each intermediate are given in the scheme.[182]

In a study of the oxidation of **57** in aqueous alkaline media using Co(sulfosalen) as catalyst, Sippola and Krause[169] found that the conversion of the substrate to the corresponding aldehyde was

highest at pH 11. The reaction was carried out at atmospheric pressure of dioxygen but, unfortunately, the best conversion they achieved was only 15.1%.

Oxidation of substituted benzylic alcohols in aqueous media with $PhI(OAc)_2$ as a terminal oxidant and chiral Mn(salen) derivatives as catalysts resulted in the kinetic resolution of the alcohols; enantiomerically enriched alcohols and carbonyl compounds were obtained as products. Conversion of the alcohols was usually about 50%, as expected, and the *ee*s of the remaining benzylic alcohols were up to 96.8%.[183]

All the reactions described above are conducted in aqueous media and all but the last reaction uses dioxygen as terminal oxidant. No hazardous organic solvents are used, and the by-products from the use of dioxygen are harmless water and H_2O_2. With our present urgent need to protect the environment, such reactions are of great interest to the chemical industry.

Mn(3,5-dichlorosalen)Cl was used to catalyse the oxidation of a wide variety of secondary benzylic alcohols to corresponding ketones with PhIO as terminal oxidant.[184] In acetonitrile reaction medium, the yields of the ketones were often almost quantitative and the reaction times short. The primary benzyl alcohol itself was much less reactive, giving benzaldehyde in only 11% yield after a long reaction time. Molecular sieves were beneficial additives in these oxidations.

Mn(salen)-catalysed oxidations of a wide variety of benzylic alcohols in a mixture of ionic liquid $[bmim]^+PF_6^-$ and CH_2Cl_2 were reported very recently.[185] Carbonyl compounds were obtained with higher efficiency than in reactions carried out in conventional organic solvents such as CH_2Cl_2 or in ionic liquid alone. Catalyst recycling was facilitated by the use of ionic liquid–CH_2Cl_2 as a reaction medium, which makes this reaction economically interesting.

The oxidation of several secondary benzylic alcohols to corresponding ketones with yields up to 99%, was recently achieved with use of $PhI(OAc)_2$ as terminal oxidant and Mn(salen)Cl complex as catalyst in CH_2Cl_2 or water as reaction medium.[186] Aliphatic alcohols were other good substrates. With water used as solvent, the method becomes an environmentally friendly one.

The oxidation of various benzylic alcohols to corresponding aldehydes and ketones was studied with use of Cr(salen)Cl as catalyst and PhIO as terminal oxidant.[187] The best conversion (93%) was obtained with benzyl alcohol. The worst conversion (26%) resulted when 2,2-dimethyl-1-phenylethanol was the substrate. The intermediately bulky benzylic alcohols gave conversions of 50 to 89%. Other non-benzylic alcohols were oxidised with good results.

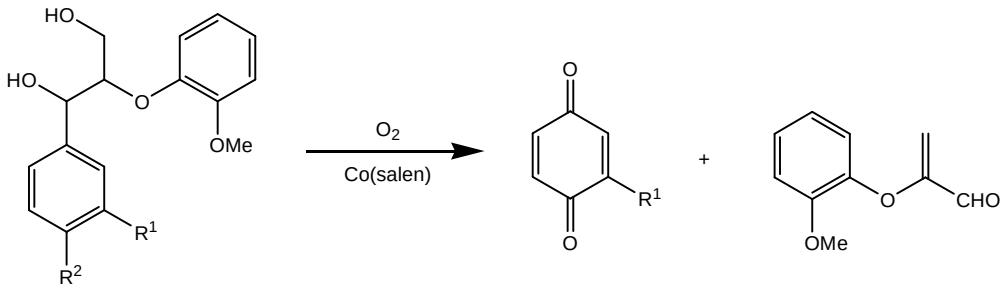
Excellent yields of carbonyl compounds were obtained by oxidising benzylic alcohols with PhIO catalysed by Cr(salen)-type complex. The reactions proceeded selectively and only aldehydes were obtained in the oxidation of primary benzyl alcohols. Relatively short reaction times were required for the oxidation.[188]

Punniyamurthy *et al.*[189, 190] used cobalt and copper complexes of tetrahydrosalen ligand to oxidise benzylic alcohols with H_2O_2. The reaction did not stop at the aldehyde stage, but rather the primary benzylic alcohols gave corresponding benzoic acids in excellent yields. Secondary benzylic alcohols gave ketones, also in excellent yields. Acetonitrile was used as solvent, and the oxidations were conducted at 80 ºC. Dioxygen was found to be an ineffective oxidant with these tetrahydrosalen catalysts.

3.2.3. Oxidation of lignin model compounds

Oxidations catalysed by salen-type complexes have rarely been investigated for lignin model compounds more complex than, for example, the substituted benzyl alcohols discussed in sections **3.2.1** and **3.2.2**. Other catalysts, such as metalloporphyrins,[191-194] metallophthalocyanines,[195, 196] transition metal salts[197] and metal complexes of macrocyclic ligands,[198, 199] have been applied, however.

Canevali *et al.*[159] studied the oxidation of dimeric lignin model compounds of arylglycerol-β-aryl ether type using dioxygen pressure of 1 MPa and Co(salen) as catalyst. Products **62-64** arising from C–C bond cleavage were obtained (Scheme 11).



59 R^1=OMe, R^2=OH
60 R^1=H, R^2=OH
61 R^1=H, R^2=OMe

62 R^1=OMe
63 R^1=H

64

Scheme 11 Oxidation of lignin model compounds of arylglycerol-β-aryl ether type.[159]

3.2.4. Oxidation of *para*-hydroxy cinnamyl alcohols

There are no publications describing the oxidation of lignin precursors, *para*-hydroxy cinnamyl alcohols, with use of transition metal complexes as catalysts. Chemical oxidations of such substrates have been carried out by using stoichiometric amounts of high-valent transition metal salts, and various amounts of polymeric and oligomeric products have been obtained.[200-204]

Enzymatic oxidations of lignin precursors have been studied extensively, on the other hand. Dehydrogenative polymers (DHPs) have been obtained[205-207] with HRP and H_2O_2.

4. AIMS OF THE STUDY

This research was funded by TEKES (Technology Development Centre of Finland) as part of the SEKAVA project (Sellun katalyyttinen valkaisu, Catalytic Bleaching of Pulps). The SEKAVA project was aimed at developing new catalysts and methods for the environmentally benign and cost-effective bleaching of pulps where the oxidants are dioxygen and H_2O_2 rather than chlorine-containing chemicals. Further funding was received from the University of Helsinki.

The objectives of my work were

1. to synthesise and structurally characterise new transition metal complexes of salen-type ligands[I, II, III, IV, V]
2. to study the catalytic oxidations of lignin model compounds and lignin precursors using these complexes as catalysts[IV,VI]
3. to prepare dehydrogenative polymers (DHPs) by chemical oxidation and compare their structures with enzymatically prepared DHPs[IV, VI]

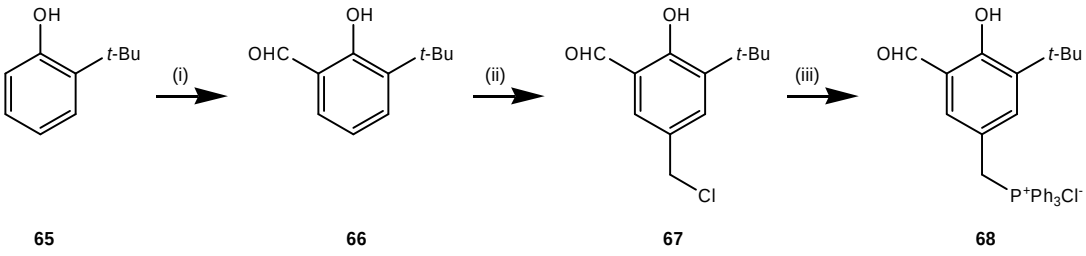
5. RESULTS AND DISCUSSION

Three types of salen complexes were synthesised: bulky phosphonium substituted complexes, complexes substituted at 5,5'-position with electron withdrawing and electron donating groups, and complexes containing tethered imidazole groups. The reactions and reaction conditions of biological systems were mimicked by carrying out oxidation experiments in aqueous solutions. Ionic complexes are desirable for this purpose because of their enhanced solubility in water.

Ammonium substituted complexes were tried to synthesise first, but in my hands the desired cationic aldehydes could not be obtained in pure form. Instead, an intractable gum was the product from several syntheses tried. Therefore a known phosphonium substituted aldehyde was chosen to prepare cationic ligands and complexes. The additional advantage of the bulky phosphonium substituents over ammoniums substituents is the enhanced solubility of the resulting complexes in organic solvents. The new complexes were tested in catalytic oxidations of lignin model compounds, 2,4,6-trichlorophenol and benzylic hydrocarbons. As well, study was made of the electronic effect of the catalysts in the rate of the oxidation of 2,5-di-*tert*-butylhydroquinone.

5.1. Phosphonium substituted salen complex

The synthesis of the phosphonium-substituted salen complexes started from 2-*tert*-butyl phenol **65** (Scheme 12), which was formylated with use of excess paraformaldehyde and a catalytic amount of $SnCl_4$ and 2,6-lutidine in toluene.[208] This method gives, selectively and in high yield, the desired product **66** where the formyl group is in *ortho*-position relative to the phenolic hydroxyl group. Other formylation methods, such as the Duff and Reimer-Tiemann formylations, give mixtures of *ortho*- and *para*-formylated products in lower yields.



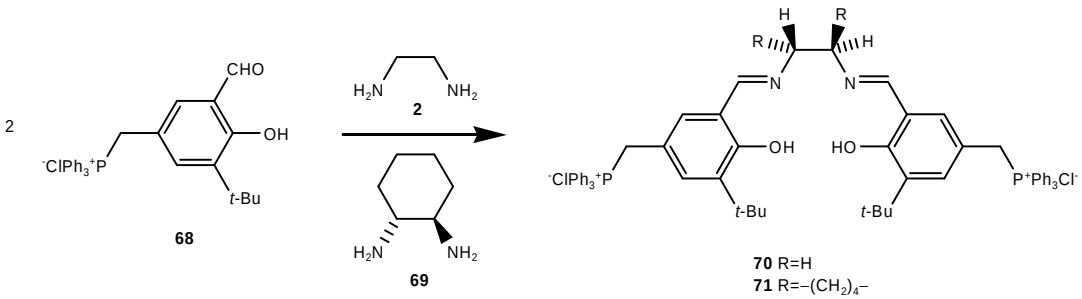
Reagents and conditions: (i) $(CH_2O)_n$, $SnCl_4$, 2,6-lutidine, toluene, 100 °C; (ii) $(CH_2O)_n$, HCl, 35 °C; (iii) PPh_3, benzene, reflux

Scheme 12 Synthesis of the phosphonium substituted aldehyde **68**.

The next step was the chloromethylation of the formylated compound **66** to **67**. In the published method,[209] this compound is synthesised by stirring **66**, paraformaldehyde and conc. HCl at room temperature for 48 h. I found, however, that the reaction did not proceed to completion under these conditions. When a slightly elevated temperature (35 °C) and prolonged reaction time (3 d) were used, compound **67** was obtained as an amber solid (mp 49-51°C) in 79% yield. In the published method it was stated that the product is a yellow oil. It was also observed that this compound was very prone to aerobic oxidation to the corresponding acid. In view of this, compound **67** was stored at -20 °C under argon atmosphere and filtered through a short silica gel column in CH_2Cl_2 to remove the acid immediately before the next reaction step.

In the next step the cationic phosphonium salt **68** was formed. Equimolar quantities of compound **67** and PPh_3 were refluxed in benzene for 5 h. After cooling to room temperature, the phosphonium salt **68** was filtered off and washed thoroughly with Et_2O to remove any starting materials. Again the literature method was found to require alteration. Although a reaction time of 1 h was reported to be sufficient,[209] I found some starting material even after 4 h of refluxing.

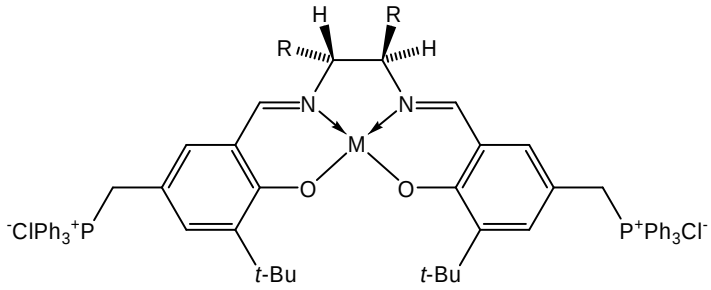
The ligands **70** and **71** were synthesised by standard methods. The aldehyde **68** (two eq.) and ethylenediamine **2** (one eq.) or (*R*,*R*)-1,2-diaminocyclohexane **69** (one eq.) were condensed in refluxing EtOH (Scheme 13). After removal of the EtOH, the ligands were obtained as yellow solids by slow evaporation of CH_2Cl_2–EtOAc solutions at room temperature. Recrystallisations were carried out by using the same method and solvents.



Scheme 13 Synthesis of ligands **70** and **71**.

Both ligands were soluble in water and in many common organic solvents excluding hydrocarbons, ethers and EtOAc. In the solid state the ligands existed as solvates, which could not be removed even by prolonged warming *in vacuo*. The solvate molecules were identified by ^{1}H NMR spectrometry and elemental analysis. Both **70** and **71** retained CH_2Cl_2, EtOAc and EtOH molecules and, in addition, compound **70** retained two H_2O molecules. In ESI mass spectra, low intensity ions corresponding to $[M–Cl]^+$ were observed, in addition to the doubly charged $[M–2Cl]^{2+}$ ions, which were the base peaks for these ligands.

The metal complexes **72**-**81** (Fig. 34) were synthesised from ligands **70** and **71** and a slight excess of metal salt in refluxing EtOH. $FeCl_2 \cdot 4H_2O$ was used for complexes **74** and **75** and metal(II)acetates for the rest of the complexes. During the syntheses, Mn^{2+} and Fe^{2+} ions were oxidized to Mn^{3+} and Fe^{3+} by aerobic oxygen.



72 R=H, M=Mn(OAc)
73 R=–(CH2)4–, M=Mn(OAc)
74 R=H, M=FeCl
75 R=–(CH2)4–, M=FeCl
76 R=H, M=Co
77 R=–(CH2)4–, M=Co
78 R=H, M=Ni
79 R=–(CH2)4–, M=Ni
80 R=H, M=Cu
81 R=–(CH2)4–, M=Cu

Fig. 34 Metal complexes **72**-**81**.

Complexes were crystallised by the same method as used for the ligands. Complexes were also obtained as solvates, retaining various amounts of CH_2Cl_2, EtOAc and water. NMR spectra were measured only from the Ni^{2+} complexes **78** and **79**. The signals were slightly broadened, but adequately resolved to support the structure. In the ESI mass spectra, low intensity ions corresponding to $[M–Cl]^+$ were obtained for all complexes except **72**, **73** and **77**. Cobalt complex **77** gave the ion $[M+H]^+$. Highly characteristic peaks corresponding to the doubly charged $[M–2Cl]^{2+}$ were observed for all complexes except **72** and **73**. Surprisingly, these manganese complexes gave ions corresponding to $[M–67]^+$. No explanation for these peaks has yet presented itself. In addition, complexes **72** and **73** revealed doubly charged $[M–Cl–OAc]^{2+}$ and triply charged $[M–2Cl–OAc]^{3+}$ ions. The structures of complexes **78**, **80** and **81** were verified by X-ray crystallography. In complex **80**, the ligand was twisted about the ethylenediamine bridge, giving distorted square planar

coordination around the Cu^{2+}-ion (Fig. 35). The nickel complex **78** had a similar structure but was less distorted (Fig. 35).

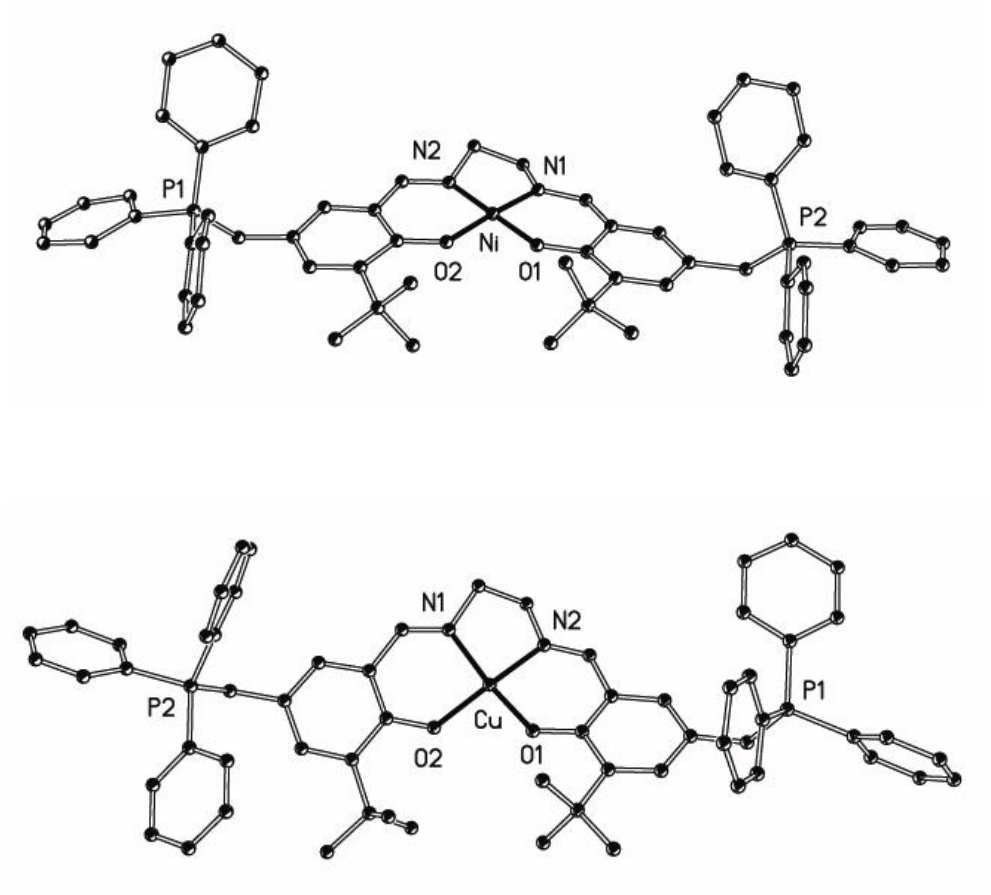


Fig. 35 Crystal structures of the complexes **78** (above) and **80** (below). Counterions and hydrogen atoms are omitted for clarity.[I]

In the chiral Cu^{2+} complex **81,** the complex cation crystallised in two different conformations.[II] In both cases, the Cu^{2+}-ions lie on the twofold axes and the geometry around them is slightly distorted square planar (Fig. 36).

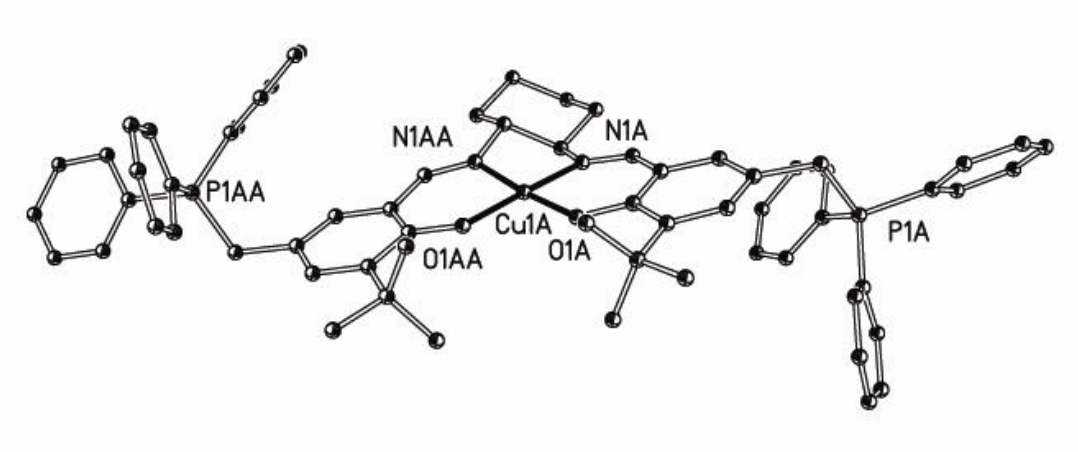


Fig. 36 Crystal structure of one of the two conformations of complex **81**. Counterions and hydrogen atoms are omitted for clarity.[II]

The crystals of complex **75** were too small for structural determination. However, crystals suitable for structural determination were obtained after ion exchange reaction reaction with an excess of NH_4PF_6 in CH_2Cl_2–EtOH solution.[III] Only the phosphonium group counterions were exchanged with the PF_6^- anions; the chloride coordinated to Fe^{3+} remained as such. In this case the coordination geometry around the Fe^{3+}-ion was square pyramidal, as expected (Fig. 37).

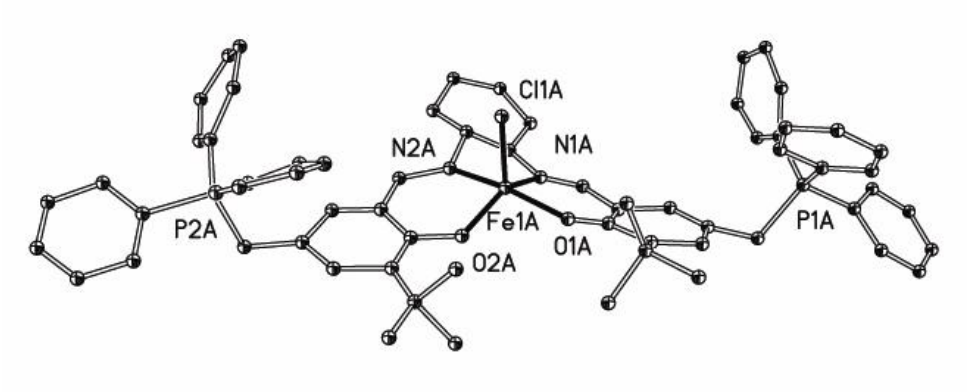


Fig. 37 Crystal structure of the PF_6^- analogue of complex **75**. Counterions and hydrogen atoms are omitted for clarity.[III]

Mn^{3+} complexes did not yield crystals of adequate quality for structure determination as such, but the ion exchange reaction with NH_4PF_6 in EtOH solution gave crystals of the PF_6^- analogue of complex **72**, in which two ethanol molecules are coordinated to manganese and the coordination around Mn^{3+} is octahedral (Fig. 38). The same complex with an excess of NH_4PF_6 and imidazole yielded crystals of bis-imidazole adduct as a PF_6^- salt.[IV] In this case, too, the coordination around Mn^{3+} is octahedral with two imidazole ligands occupying the apical positions (Fig. 38). Unfortunately, the quality of the crystal data was low in this case. So far, the cobalt complexes **76** and **77** have resisted all attempts to grow crystals suitable for X-ray crystallography.

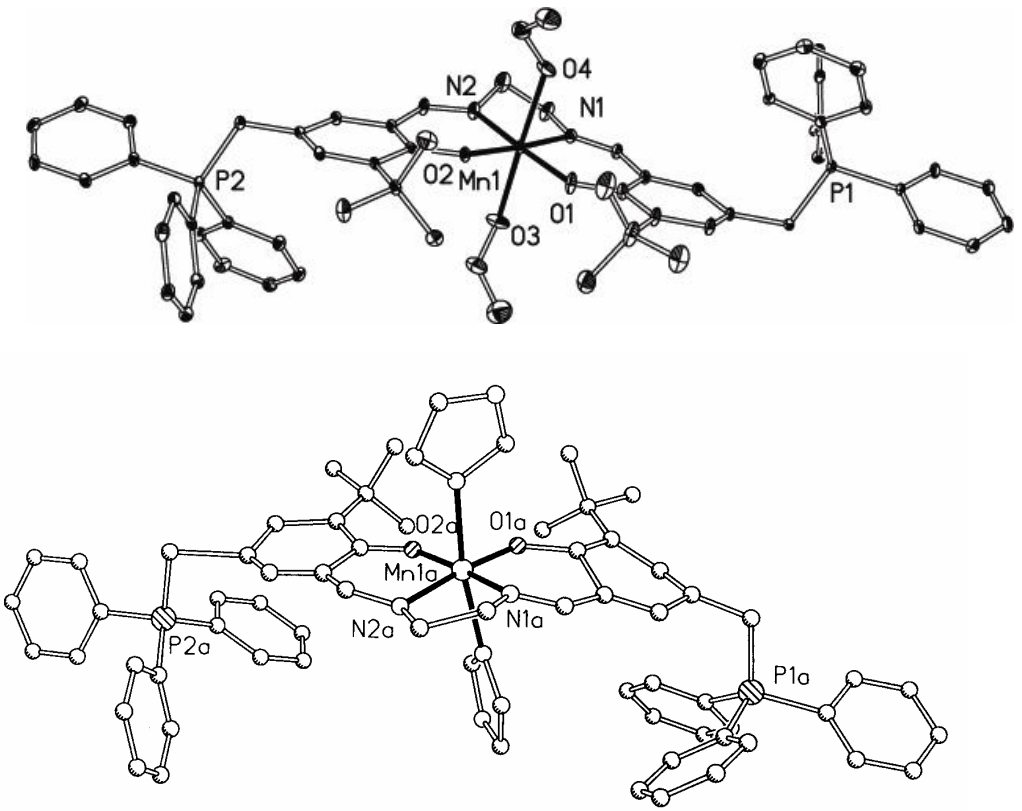
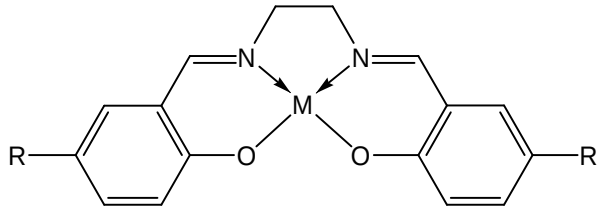


Fig. 38 Crystal structures of the two derivatives of complex **72**. Above is the bis-ethanol adduct and below the bis-imidazole adduct.[IV] Hydrogen atoms and counterions are omitted for clarity.

5.2. 5,5'-Substituted salen complexes

To allow a systematic study of the electronic effects of the complexes in catalytic oxidations, I synthesised a series of compounds bearing different substituents at 5- and 5'-positions. The substituents ranged from the electron donating $-NMe_2$ to the strongly electron withdrawing $-NO_2$ (Fig. 39).

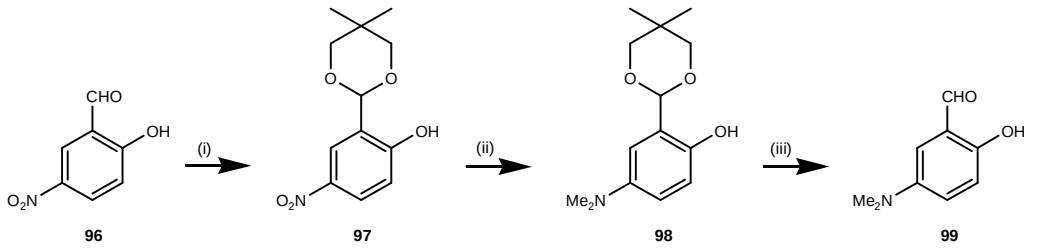


82 R=NMe_2, M=MnCl
83 R=OMe, M=MnCl
84 R=Me, M=MnCl
85 R=H, M=MnCl
86 R=Br, M=MnCl
87 R=SO_3Na, M=Mn
88 R=NO_2, M=MnCl
89 R=NMe_2, M=Co
90 R=OMe, M=Co
91 R=Me, M=Co
92 R=H, M=Co
93 R=Br, M=Co
94 R=SO_3Na, M=Co
95 R=NO_2, M=Co

Fig. 39 5,5'-Substituted salen complexes **82-95**.

The aldehydes used in the ligand preparations were commercial products or were synthesised by the literature procedures.[45, 208, 210, 211] Aldehyde **99**, needed for the preparation of **82** and **89**, has been reported earlier,[212] but the synthetic procedure described failed to give the desired product. An alternative method was then developed, where the aldehyde group of **96** was protected as an acetal

97 derived from 2,2'-dimethyl-1,3-propanediol during the reductive alkylation of the nitro group yielding **98**. After the hydrolysis of the protective group, aldehyde **99** was obtained as a yellow oil (Scheme 14).



96 **97** **98** **99**

Reagents and conditions: (i) 2,2-dimethyl-1,3-propanediol, *p*-TsOH, toluene, reflux; (ii) 1 atm H_2, Pd/C, formaldehyde, EtOH, rt; (iii) 2M HCl, Na_2CO_3, rt

Scheme 14 Synthesis of aldehyde **99**.

The ligands for the complexes **83-86**, **88**, **90-93** and **95** were synthesised by condensing two eq. of the appropriate aldehyde with one eq. of ethylenediamine in refluxing EtOH. The sulfonated aldehyde needed for complexes **87** and **94** was insoluble in EtOH and therefore the condensation reaction was carried out in EtOH–H_2O mixture. After the addition of a small amount of distilled water to the ethanolic reaction mixture, the desired diimine precipitated in adequate purity for the complexation step. The sulfonated ligand was obtained directly from the reaction mixture by filtering it out.

The Mn^{3+} complexes **83-86** and **88** were synthesised by standard methods. Usually this involved refluxing the ligand with two eq. of $Mn(OAc)_2 \cdot 4H_2O$ in EtOH for a few hours followed by counterion exchange with three eq. of LiCl. After the addition of a small amount of water, dark brown complexes precipitated. The complex **87** was isolated as Mn^{2+} species. The complex **82** was synthesised without the isolation of the ligand, by mixing appropriate amounts of the aldehyde **99**,

ethylenediamine, $Mn(OAc)_2 \cdot 4H_2O$ and LiCl in refluxing EtOH. The attempted synthesis of the NMe_2-substituted ligand by standard procedure failed to yield the desired product. Instead, a red oil yielding complicated NMR spectra was obtained. The complex **82** prepared by one-pot method could not be unambiguously characterised, possibly due to the impurities, but the mass spectrum of the preparation indicated that the desired compound was the main species.

In all cases except complex **87**, the Mn^{2+} ions were oxidised to Mn^{3+} ions by atmospheric oxygen. This commonly happens in the synthesis of salen complexes of manganese. Mn^{2+} was not oxidised in the case of complex **87**, presumably because the initially formed Mn^{2+} complex was poorly soluble in the reaction medium and did not react further with oxygen during the short reaction time. It was found by mass spectrometry that the complex **87** could be stored in atmospheric conditions for at least several years as a solid without the Mn^{2+} being oxidised to Mn^{3+}. An unusual reaction was observed in the case of the unsubstituted Mn(salen)Cl **85** during crystallisation from pyridine in aerobic conditions. The Mn^{3+} ions were reduced, probably with the pyridine solvent, and the binuclear Mn^{2+} complex, bridged by the phenolato oxygens, was isolated and characterised by X-ray crystallography (Fig. 40).[V] This is unusual, because the salen-type manganese complexes are prone to aerobic oxidation and usually exist as Mn^{3+} compounds unless they are prepared under an inert atmosphere. The complexes were characterised by mass spectrometry.

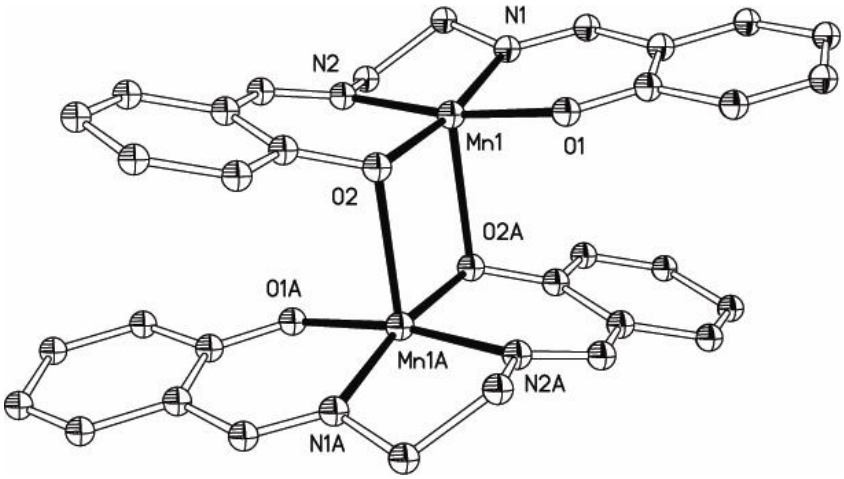


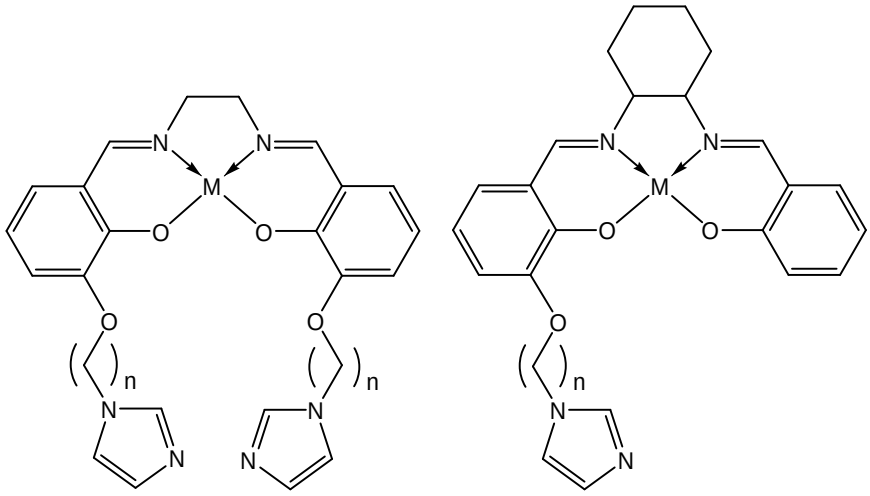
Fig. 40 Crystal structure of the binuclear reduction product of complex **85**. Hydrogen atoms are omitted for clarity.[V]

The Co^{2+} complexes **90**-**93** and **95** were synthesised by refluxing the ligand and two eq. of $Co(OAc)_2 \cdot 4H_2O$ in EtOH. After the addition of a small amount of water to the reaction mixture, brownish-black complexes were isolated by filtration. The sulfonated complex **94** was synthesised in EtOH–H_2O mixture, like the corresponding manganese complex **87**. Complex **89** was synthesised by one-pot method without isolation of the ligand, like the manganese complex **82**. The preparation of **89** was similarly impure.

Unlike the Mn complexes, in all Co complexes the central metal ion existed in oxidation state +2. The oxidation of Co^{2+} with atmospheric oxygen during complexation is rarely encountered; usually some other oxidant, such as H_2O_2, halogens or alkyl hydroperoxides, is needed to convert the Co^{2+} to Co^{3+}.

5.3. Salen complexes with tethered imidazole groups

Enzymes LiP and MnP have a haeme prosthetic group. In addition to the four nitrogens of the porphyrin ring, an additional fifth nitrogen from an axially coordinating histidine residue binds to the central iron ion.[58] This axial ligand has a pronounced effect on the structures and functions of these and other enzymes. To mimic the effect of this ligand, I synthesised salen complexes having alkyloxyimidazole substituents in the ligand backbones (Fig. 41). The idea was that these imidazolyl residues would coordinate to the apical positions and form five- or six-coordinated species. Similar salen-[68, 69] and porphyrin-[213, 214] type complexes have been synthesised earlier and often they exhibit enhanced catalytic activities relative to complexes having no such "tail".



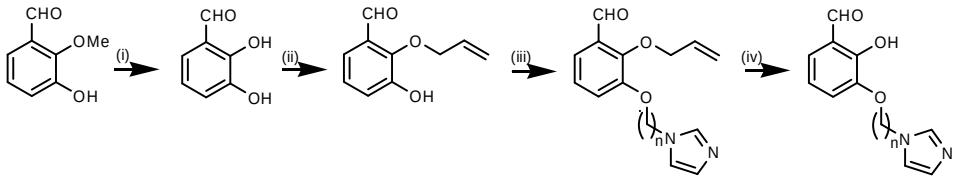
100 n=3, M=Mn
101 n=4, M=Mn

102 n=3, M=Mn$(PF_6)^-$
103 n=4, M=Mn$(PF_6)^-$

Fig. 41 Complexes **100**-**103** containing tethered imidazole groups.

For the synthesis of these complexes, aldehydes **109** and **110** bearing the imidazole-containing tail were needed. They were synthesised starting from the o-vanillin **104** by demethylation to **105**,[215]

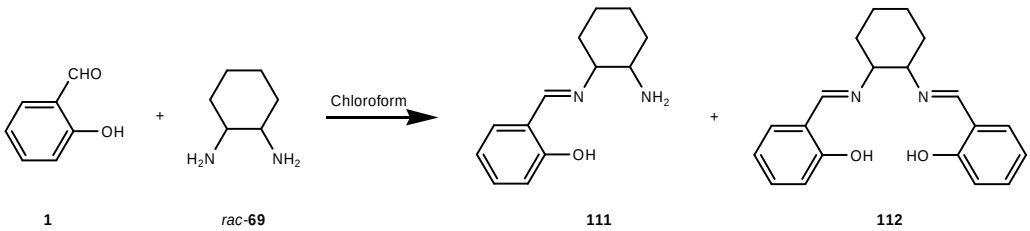
selective allylation yielding **106**,[216] an ether synthesis with 1-(ω-bromoalkyl)-imidazoles (prepared by the method described in ref. 217 with slight modifications) yielding **107** and **108** and finally deallylation yielding **109** and **110**[218] (Scheme 15).



Reagents and conditions: (i) HBr, AcOH, reflux; (ii) NaH, allyl bromide, DMSO, rt; (iii) NaH, 1-(ω-bromoalkyl)-imidazole, DMF, rt; (iv) $Pd(OAc)_2$, PPh_3, Et_3N, HCOOH, 80 % EtOH, reflux

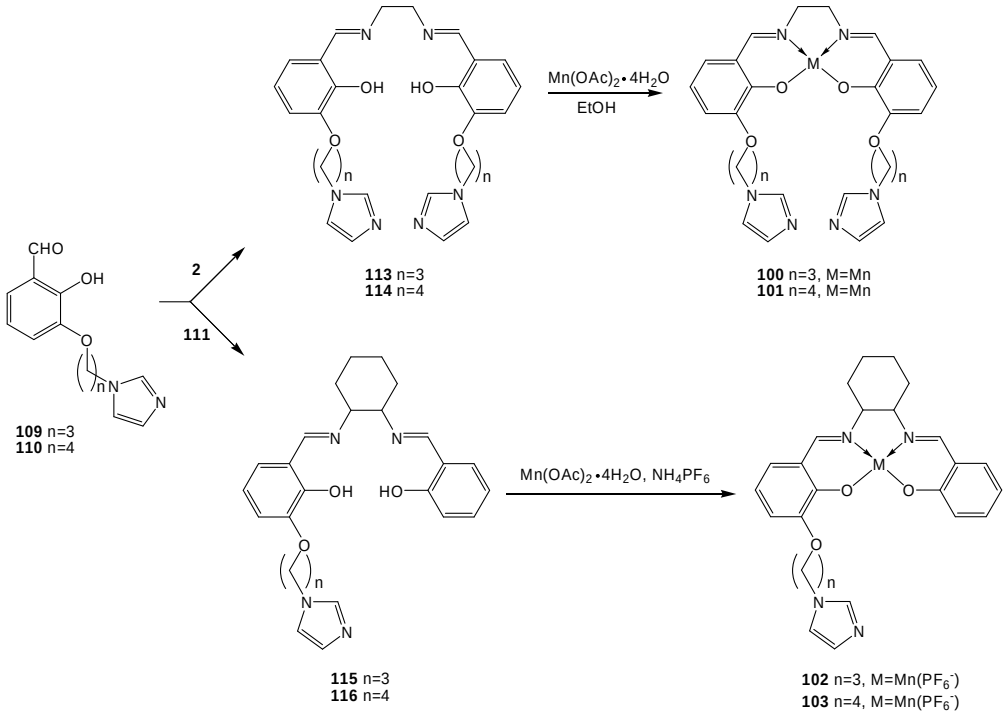
Scheme 15 Synthesis of the aldehydes **109** and **110**.

A preformed monoimine **111** was required for the "monotailed" complexes **102** and **103**. This was synthesised from salicylaldehyde **1** and (±)-1,2-diaminocyclohexane (*rac*-**69**) (Scheme 16). In the published synthesis, it is claimed that **111** forms in 95% yield and in high purity.[219] I was unable to duplicate this result: the yield of **111** was only 26%, and dry-column chromatography was required to remove the diimine **112**, which was the major product. The published NMR data clearly indicate that the mixture had been obtained earlier as well.



Scheme 16 Synthesis of monoimine **111**.

The condensation of aldehydes **109** and **110** with ethylenediamine **2** or monoimine **111** yielded the desired "tailed" ligands **113-116**. Treatment of these with $Mn(OAc)_2 \cdot 4H_2O$ in refluxing EtOH gave the complexes **100** and **101**. For complexes **102** and **103**, treatment with an excess of NH_4PF_6 in MeOH followed by addition of H_2O was used to convert the acetato complexes to PF_6^- complexes (Scheme 17).

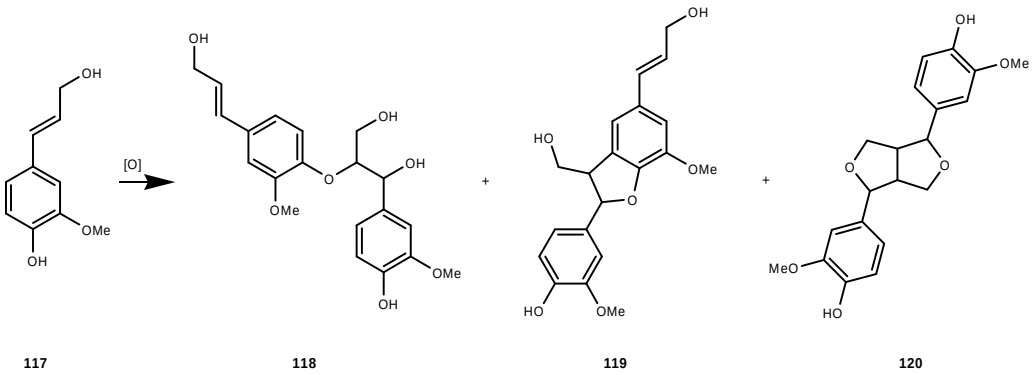


Scheme 17 Synthesis of complexes **100-103** with one or two tethered imidazole groups.

5.4. Biomimetic oxidations of coniferyl alcohol, a lignin precursor

Oxidative enzymes such as lignin peroxidase (LiP), manganese peroxidase (MnP) and laccase participate in the bioconversions of lignin. The capability of the salen-type metal complexes to function as mimics for these enzymes was tested by oxidising coniferyl alcohol **117** with H_2O_2 or

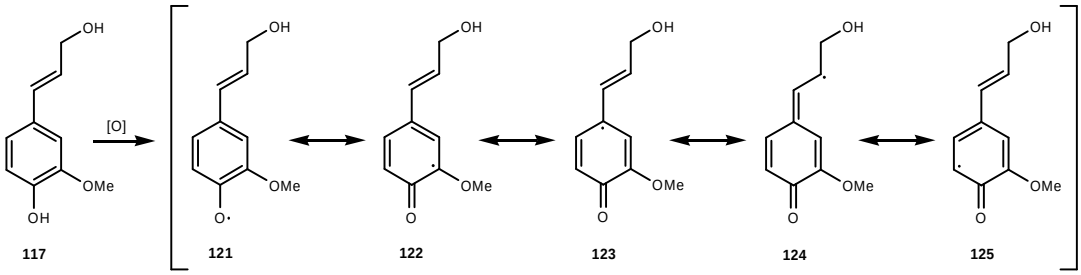
O_2 catalysed by the prepared complexes.[IV, VI] The oxidations were carried out at room temperature in buffered aqueous dioxane solutions at pH 3 and 6. The reactions were quenched after the starting material was consumed. The oxidation products consisted of mixtures of coniferyl alcohol dimers, oligomers and polymers in various proportions. The main products were β–O–4, β–5 and β–β dimers **118-120** (Scheme 18). The amounts of these products were determined from the NMR spectra of the acetylated reaction products.



117 **118** **119** **120**

Scheme 18 Formation of products **118-120** by the oxidative coupling of **117**.

The one-electron oxidation of **117** leads to the formation of resonance-stabilised radicals **121-125** (Scheme 19). The coupling of these radicals gives the products **118-120**. These reactions are also the initial steps in the formation of lignin during the biosynthesis of this macromolecule in plants. In lignin biosynthesis the macromolecular structure is formed by further coupling of phenoxy radicals **121-125** with the growing lignin precursor.



Scheme 19 Formation of radicals **121-125** by the one-electron oxidation of **117**.

Compounds **118**, **119** and **120** are formed by coupling of radicals **121** and **124**, **124** and **125** and two radicals of **124**, respectively. Some minor structural components in oxidation mixtures and in lignins are formed by other radical couplings, but their amount is usually low.

The results obtained in oxidations of **117** with use of H_2O_2 or O_2 as oxidant and salen-type transition metal complexes as catalyst depended on the oxidant and catalyst as well as on the reaction conditions, such as pH. The results were compared with those obtained with the HRP enzyme as catalyst. The following tables present the reaction times and relative amounts of products **118-120**.

Table 2 Results obtained in the oxidation of **117** at pH 3.

Catalyst	Oxidant	**118**[a]	**119**[a]	**120**[a]	Time[b]	Polymerisation
72, **73**	H_2O_2	1	1	1	40 min	oligomeric
74, **75**	H_2O_2	1	1	1	2 h	oligomeric
76, **77**	O_2	1	2	3	1 h	dimeric
80, **81**	H_2O_2	1	1	1	3 d	dimeric
85, **87**	H_2O_2	1	2	3	18 h	oligomeric
92	O_2	1	3	3	12 h	dimeric
HRP	H_2O_2	1.5	1	1	1 h	oligomeric

[a] The relative amounts of **118**-**120** were determined from NMR spectra.

[b] Disappearance of **117** was determined by TLC.

Table 3 Results obtained in the oxidation of **117** at pH 6.

Catalyst	Oxidant	**118**[a]	**119**[a]	**120**[a]	Time[b]	Polymerisation
72, **73**	H_2O_2	1	1	1	15 min	polymeric
74, **75**	H_2O_2	1	1	1	45 min	polymeric
76, **77**	O_2	1	2	3	45 min	dimeric
80, **81**	H_2O_2	1	1	1	2 d	dimeric
85, **87**	H_2O_2	1	2	3	2 h	oligomeric
92	O_2	1	3	3	5 h	dimeric
HRP	H_2O_2	1	1	1	45 min	polymeric

[a] The relative amounts of **118**-**120** were determined from NMR spectra.

[b] Disappearance of **117** was determined by TLC.

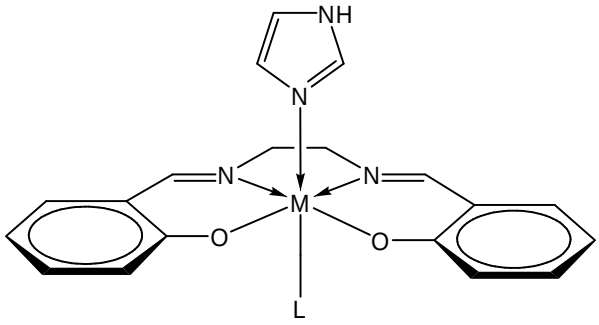
Tables 2 and 3 show that the sterically bulky complexes **72-75** and HRP exhibit similar regiochemistry in the coupling reaction. HRP-catalysed oxidations are thought to proceed without an interaction between the catalyst and the phenoxy radicals in the coupling step itself.[220] According to my results, the bulky complexes **72-75** show a similar lack of interaction. The less bulky catalysts **85** and **87** gave markedly different product distributions from **72-75** in the H_2O_2 oxidations. The O_2 oxidations catalysed by bulky **76** and **77** and by the less bulky **92** showed similar regiochemistries, suggesting that these complexes have a similar interaction with the phenoxy radical in the coupling step.

The degree of polymerisation in the experiments varied consiberably. Cobalt and copper complexes gave mainly dimeric products, whereas all iron and manganese complexes, as well as HRP, gave material with a higher degree of polymerisation, ranging from oligomeric to polymeric.

Increasing the pH of the reaction mixture from pH 3 to pH 6 in most cases markedly increased the reaction rate. This is because, at higher pH, more of the phenolic OH groups are deprotonated to more easily oxidised phenolates.

LiP and MnP both contain an axially coordinating histidine residue bound to the heme iron ion.[58] In addition, catalytic oxidations with salen-type catalysts benefit from the addition of some kind of axially coordinating ligand.[62, 63]

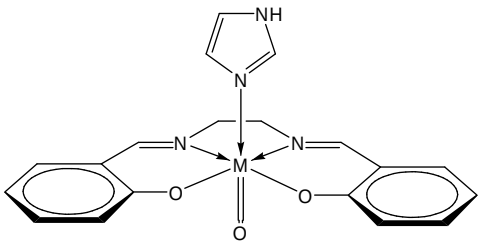
The effect of a *N*-coordinating axial ligand was tested by conducting the oxidations in the presence of imidazole,[IV] which occupies the vacant axial site in square planar or square pyramidal salen-type transition metal complexes, forming a new compound with a structure like **126** (Fig. 42).



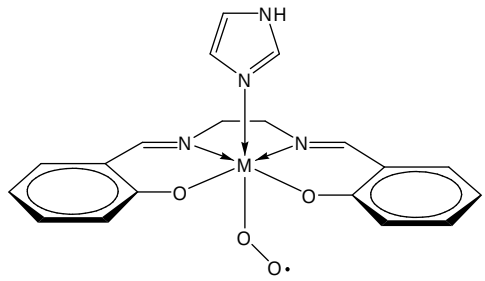
126

Fig. 42 Structure **126** with axially coordinated imidazole. L=ligand or vacant site.

The axially coordinating ligand facilitates the formation of the actual oxidising species, which in the case of manganese complexes is a metal-oxo complex of the type **127**, and in the case of cobalt complexes usually a metal-superoxo complex like **128** (Fig. 43). Metal-peroxo complexes also exist when the metal is cobalt. To date, the metal-oxo complexes having a salen-type ligand and manganese as a metal have not been crystallographically characterised, but mass spectral studies have demonstrated the existence of these structures.[143, 145, 154] Also, X-ray structures for Mn^{5+}-oxo complexes bearing N_4-coordinating tetra-amido type ligands have been obtained.[120, 121] Several Co^{3+}-superoxo complexes having salen-type ligands have been structurally characterised.[105, 126, 221]



127



128

Fig. 43 Structures of metal-oxo (**127**) and metal-superoxo (**128**) salen complexes with coordinated imidazole in the second apical position.

Table 4 shows the results obtained in the oxidation of **117** with added imidazole. The reaction conditions were otherwise the same as in the reactions in Table 2, but 50 mol-% imidazole, relative to the substrate, was added to the reaction mixture to function as a cocatalyst.

Table 4 Effect of the imidazole on the oxidation of **117**.

Catalyst	Oxidant	**118**[a]	**119**[a]	**120**[a]	Time[b]	Polymerisation
72, **73**	H_2O_2	1	1	1	30 min	oligomeric
74, **75**	H_2O_2	1	1	1	30 min	oligomeric
76, **77**	O_2	–	–	–	–[c]	–
80, **81**	H_2O_2	–	–	–	–[c]	–
85, **87**	H_2O_2	1	2	3	1 h	oligomeric
92	O_2	–	–	–	–[c]	–

[a] The relative amounts of **118**-**120** were determined from NMR spectra.

[b] Disappearance of **117** was determined by TLC.

[c] No reaction.

In the case of manganese and iron complexes as catalysts and H_2O_2 as oxidant, the addition of imidazole increases the reaction rate (Table 4). Imidazole completely inactivates cobalt and copper catalysts, however, possibly due to the too strong coordination to the metal ion, which renders the catalyst unable to coordinate oxygen species.

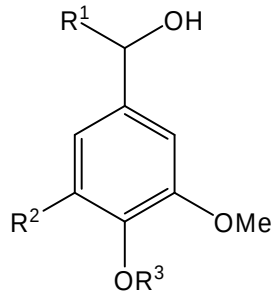
The reaction mechanism of the oxidation of phenols with O_2 catalysed by Co complexes has been studied since the 1960s, and several different mechanisms have been published. Some of these reactions involve the transfer of oxygen atom to the substrate while others involve only electron transfer reactions. The mechanism for the oxidation of phenols using Mn complexes as catalysts is largely unstudied. In the present study, minimal oxygen atom transfer was detected in oxidations with either Co or Mn complexes. The fate of the oxygen species bound to the metal in the active oxidant was not studied. However, this oxygen species must be removed from the metal to regenerate the catalyst for further reactions.

5.5. Catalytic oxidation of phenolic and non-phenolic benzylic alcohols

In this study, a variety of phenolic and non-phenolic benzylic alcohols, which are very simple lignin model compounds, were catalytically oxidised with metallosalen complexes as catalysts and H_2O_2 as terminal oxidant.[IV, VI]

The general reactivity of these substrates was studied by first preparing a series of substituted benzylic alcohols **129**-**136** (Fig. 44). Compounds **129** and **130** were obtained commercially, and compounds **131**-**133** were synthesised by literature methods.[222-224] Compounds **134** and **136** were prepared from compounds **133** and **135** with excess of MeI and K_2CO_3 in acetone. The method reported for **135**[225] failed to give the desired product, but compound **135** was succesfully synthesised, albeit in low yield, from benzylated **133** and methylmagnesium iodide in anhydrous

Et_2O. Surprisingly, the benzyl group was cleaved during the reaction and **135** was isolated directly after the Grignard reaction, without the need of an additional hydrogenolysis step.



129 R^1=R^2=R^3=H
130 R^1=R^2=H, R^3=Me
131 R^1=Me, R^2=R^3=H
132 R^1=R^3=Me, R^2=H
133 R^1=R^3=H, R^2=OMe
134 R^1=H, R^2=OMe, R^3=Me
135 R^1=Me, R^2=OMe, R^3=H
136 R^1=R^3=Me, R^2=OMe

Fig. 44 Benzylic alcohols **129**-**136** used as substrates in catalytic oxidations.

The benzyl alcohols **129**-**136** were oxidised using **87** (5 mol-%) as catalyst and H_2O_2 (3 eq.) as oxidant in alkaline (pH 10) MeOH–H_2O (1:1) solution at room temperature. The reactions were allowed to proceed overnight. The product mixture consisted of various amounts of starting materials and corresponding carbonyl compounds. The only compound not oxidized at all was **131**. The results of the oxidations are compiled in Table 5. In no cases were carboxylic acids or C–C coupled or C–O coupled products detected.

Table 3. Results obtained in oxidations of **129**-**136** with H_2O_2 catalysed by **87**.

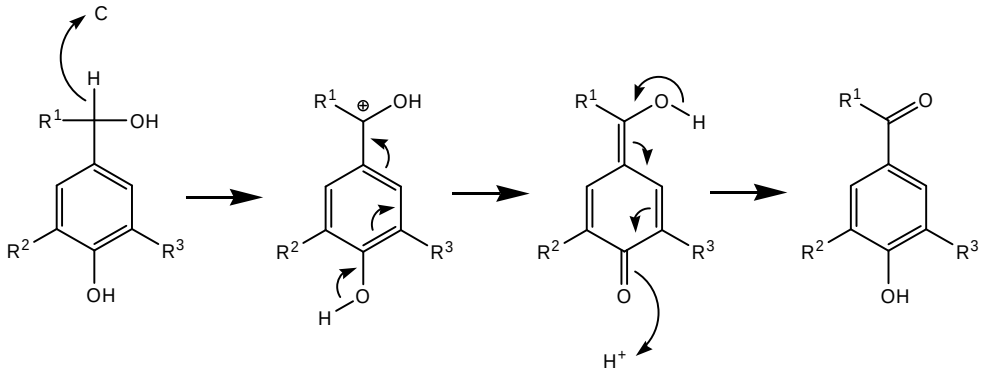
Substrate	Yield (%)
129	70
130	65
131	0
132	52
133	100
134	21
135	100
146	35

Table 5 shows that, in general, the phenolic compounds **129**, **133** and **135** are oxidised in higher yields than the corresponding non-phenolic compounds, except compound **131**. For phenolic compounds, the yields are higher for 3,5-dimethoxylated compounds **133** and **135** than for 3-methoxylated compounds **129** and **131**. For non-phenolic compounds, the trend is the opposite: the 3-methoxylated compounds give higher yields than the 3,5-dimethoxylated ones.

Where the reaction did not proceed to completion, an additional amount of oxidant and/or catalyst was added. Surprisingly, these additions had no effect on the yields. This inactivation of the system may be due to metal ions which are liberated to the solution by decomposition of the catalyst. These ions could form some kind of inactive, bimetallic species, inactivating the system for further oxidation.

The compound **131** showed very strange behaviour in oxidation. In addition to the above catalytic oxidation system, **131** was inert when potassium peroxydisulfate, cerium ammonium nitrate or potassium dichromate was used as oxidant. Of the oxidants tested, only potassium permanganate was able to oxidise **131**, yielding the corresponding ketone as product.

For the above oxidations of phenolic benzyl alcohols, a reaction mechanism resembling that given[226] for oxidations with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) as stoichiometric oxidant is postulated. First, the catalytically active species removes a hydride ion from the benzylic position. The resulting cation loses a proton, and after tautomerisation the oxidised product is obtained (Scheme 20). Since the only observed products were aldehydes and ketones, the reaction appears to be a two-electron oxidation.



137 **138** **139** **140**

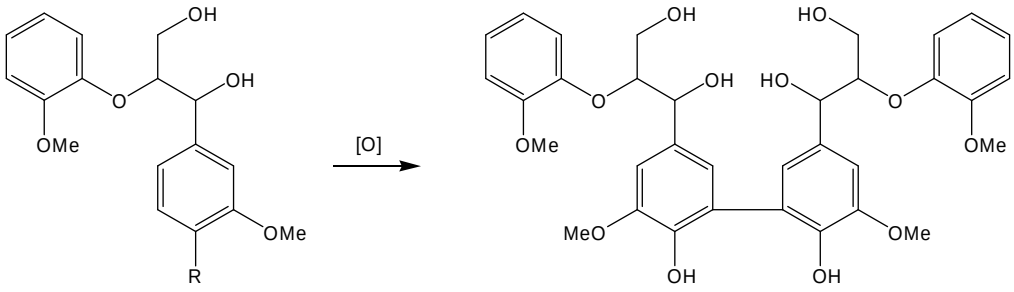
C=Catalytically active species, possibly metal-oxo or metal-superoxo complex

Scheme 20 Postulated mechanism for the oxidation of phenolic benzylic alcohols.

5.6. Catalytic oxidation of more complex lignin model compounds

Oxidations of dimeric lignin model compounds were conducted[IV] to test the ability of the metallosalen complexes to degrade lignin-like material. These oxidations were carried out at room temperature in MeOH–H_2O (1:1) buffered to pH 10, with 5 mol-% of the catalyst and H_2O_2 or O_2 as oxidant.

Dimeric β–O–4 lignin model compounds 2-(2-methoxyphenoxy)-1-(4-hydroxy-3-methoxyphenyl)-1,3-propanediol **141** and 2-(2-methoxyphenoxy)-1-(3,4-dimethoxyphenyl)-1,3-propanediol **142** were the first model compounds to be tested (prepared by the method described in ref. 227). In H_2O_2 oxidations catalysed by complexes **72**, **85** and **87**, phenolic model compound **141** was oxidatively coupled to form the tetrameric C–C coupled compound **143** in quantitative yield, but **142** did not react (Scheme 21). With cobalt complexes as catalysts and dioxygen as terminal oxidant, both **141** and **142** were unreactive; the starting material was recovered quantitatively. The corresponding carbonyl compounds were not detected in the oxidations and, indeed, **143** was the only product identified. Identification was based on the NMR and mass spectra and comparison with an authentic sample.[228, 229] No evidence was obtained for the desired C_α–C_β-bond cleavage. From the NMR spectra and solubility differences, it was presumed that **143** exists as a mixture of atropisomers. Supporting the observed results, computational studies[230] indicate that there is a considerable energy barrier between the two atropisomers.



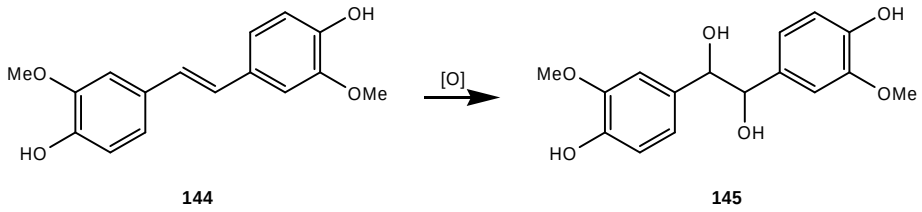
141 R=OH
142 R=OMe

143

Scheme 21 Model compounds **141** and **142**, and the C–C coupled product **143**.

The degradation of **141**, with formation of 1,4-benzoquinone **62** and unsaturated aldehyde **64** as products, has been achieved at 1MPa pressure by using Co(salen) as catalyst and dioxygen as oxidant[159] (see Scheme 11). Oxidation of non-phenolic model compound **142** with substituted *meso*-tetraarylporphyrin complexes as catalysts and $KHSO_5$ as terminal oxidant yields benzaldehyde **58** and 1,4-benzoquinone **62** as products.[192, 231]

The residual lignin found in chemical pulps contains chromophoric structures in addition to the common β–O–4 type structures. The chromophoric model compound used in this study was *E*-4,4'-dihydroxy-3,3'-dimethoxystilbene **144**, and the oxidation of **144** with **87** as catalyst and H_2O_2 as oxidant in pH 10 MeOH–H_2O (1:1) gave diol **145** in almost quantitative yield (Scheme 22).[VI] The diol **145** was most probably formed *via* an epoxide intermediate followed by ring-opening in alkaline medium. No cleavage of the double bond or oxidation of the phenolic moieties was observed.



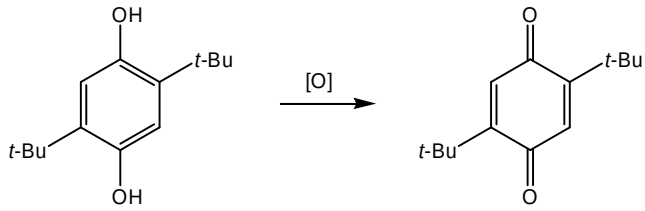
144 **145**

Scheme 22 Oxidation of stilbene **144** to diol **145**.

On the other hand, when **94** was used as catalyst and dioxygen as oxidant in refluxing MeOH–H_2O, the double bond of **144** was cleaved, yielding vanillin in good yield. Of all the oxidations I studied, the oxidations of compound **144** were the only ones where oxygen atom transfer from the active catalyst to the substrate was evident.

5.7. Electronic effects of the catalyst on the oxidation

The electronic effects of the ligands in the oxidation capacity of salen complexes have been extensively studied for of the epoxidation of alkenes[2b, 62, 141, 232-234] and the oxidation of sulfides to sulfoxides.[235-237] These studies have shown that complexes bearing electron withdrawing substituents give the fastest reactions. Evidently only one study has been conducted on phenol oxidation. Varying the substituents in Co(*N*-Me-salprn)-type complexes was found to have only a very minor effect on the reaction rate in the oxidation of 2,6-disubstituted phenols with dioxygen as oxidant.[238] Since manganese catalysts have not been studied in this way, I synthesised a number of complexes (**83**-**88**) bearing electron donating and electron withdrawing substituents in the ligands and tested them in the oxidation of 2,5-di-*tert*-butylhydroquinone **146**. Substrate **146** was chosen because it gives only one oxidation product, 2,5-di-*tert*-butylbenzoquinone **147** (Scheme 23). Following the oxidation by UV-Vis spectrometry was thus an easy task.



146 **147**

Scheme 23 Oxidation of **146** to **147**.

The manganese complexes **83-88** were studied with H_2O_2 as oxidant in MeOH. A large excess of H_2O_2 (100 eq. relative to the substrate) was used so that the availability of oxidant would not limit the reaction rate. The disappearance of the starting material was followed by measuring the absorbance of the reaction mixture at 288 nm in a 10-mm quartz cuvette. At this wavelength neither catalysts nor other species in the reaction mixture interfered with the measurements. Measurements were conducted at three minute intervals and reactions were followed for 42 min in total. The initial relative reaction rates were determined by the change of absorbance during the first three minutes (Fig. 45). The complexes with strongest electron-donating substituents gave the fastest reaction rates. The rate of the reaction declined steadily with substituents that were more electron withdrawing. For most of the catalysts, the reaction was essentially completed in 15 min. In the case of catalyst **83**, little oxidation was apparent after the first three minutes. The most steady reaction rate during the 42 min period was with catalyst **87**. These results suggest that, in phenol oxidations with H_2O_2 as the oxidant, the trend is opposite to that observed for alkene epoxidations and sulfide oxidations. The probable explanation is the different reaction mechanism. Alkene epoxidation and oxidation of sulfides to sulfoxides involves an oxygen atom transfer from the active oxidant to the substrate, whereas the oxidation of phenols involves radical-like reactions, initiated by hydrogen atom abstraction from the phenolic OH group.

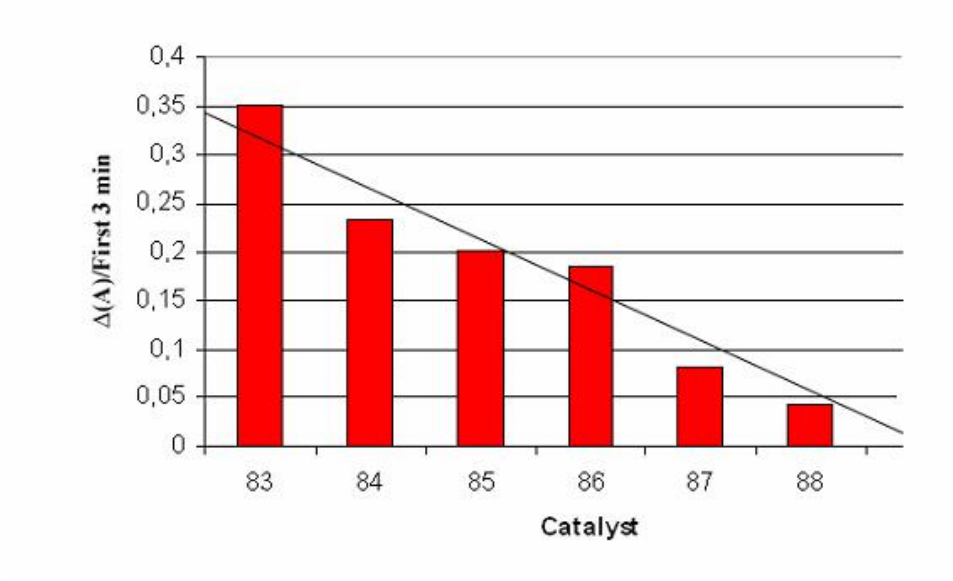


Figure 45 Changes in absorbances at 288 nm during the first three minutes in the oxidation of **146** with H_2O_2 and catalysts **83**-**88**.

5.8. Other oxidations

The ability of the complex **100** to catalyse the oxidation of 2,4,6-trichlorophenol and benzylic hydrocarbons was tested. The phenolic substrate was oxidised with 5 mol-% of the catalyst and 3 eq. of H_2O_2 as terminal oxidant in aqueous acetonitrile solution (1:9) at room temperature. The substrate was quickly (< 1h) consumed, and a small amount of degradation product, 2,6-dichloro-1,4-benzoquinone, was obtained along with larger amounts of dimeric and oligomeric coupling products of characteristic purple colour.[239]

Ethylbenzene, propylbenzene and diphenylmethane were the substrates in the study of the oxidation of benzylic hydrocarbons. With H_2O_2 as oxidant and complex **100** as catalyst, yields of the oxidation products were very low. On the other hand, when monoperoxysulfates soluble in organic solvents, namely Bu_4NHSO_5 and Ph_4PHSO_5, were used as oxidants, the combined yields of

the benzylic alcohols and ketones were about 50%. Ketones were the main products in all cases, amounting to about 80% of the oxidised products for ethylbenzene and propylbenzene. Diphenylmethane with its highly activated benzylic position gave the corresponding ketone in 85% yield with no alcohol detected. The oxidations of hydrocarbons were carried out in acetonitrile solution with 5 mol-% of **100** and 3 eq. of the oxidant at room temperature. Similar results have been obtained with PhIO and NaOCl as oxidants.[5]

6. CONCLUSIONS

A novel class of cationic phosphonium substituted salen complexes of first-row transition metals were synthesised and characterised. These complexes are soluble both in water and in organic solvents, which permits their reactivity to be studied under a wide variety of conditions. The manganese and iron complexes **72-75** proved to be efficient oxidation catalysts for phenols, benzylic alcohols and lignin model compounds with H_2O_2 or other peroxides as terminal oxidants. Salen complexes with tethered, intermolecularly coordinating imidazole groups were also synthesised.

The manganese complex **100** was found by X-ray crystallography to form a coordination polymer in the solid state. The coordination around manganese ions in this complex is octahedral, the imidazole nitrogens coordinating to apical positions. Most likely the coordination of the imidazole groups is labile in solution. This was deduced from the finding that complex **100** is a highly efficient oxidation catalyst. With H_2O_2 as terminal oxidant, it is capable of catalysing the oxidative degradation of 2,4,6-trichlorophenol, pollutant resistant to biological degradation. Oxidation of the benzylic positions of hydrocarbons catalysed by **100** was studied, and the corresponding alcohols and ketones were produced in fair yields, especially with monoperoxysulfates as terminal oxidants.

During the attempted preparation of X-ray quality crystals of Mn(salen)Cl **85** by slow evaporation of the pyridine solution of the complex, a very unusual reduction of Mn^{3+} to Mn^{2+} was observed, yielding binuclear complex bridged by phenolato oxygens. Under aerobic conditions, salen complexes of manganese have a strong tendency to exist in Mn^{3+} oxidation state.

A method was developed for oxidising benzylic alcohols in neutral and alkaline aqueous media. Both phenolic and non-phenolic benzylic alcohols were converted to the corresponding aldehydes and ketones, usually in good yields, by oxidation with H_2O_2 catalysed by manganese complexes. The substitution pattern of the substrate had a huge impact on the reaction. Quantitative yields were obtained with syringyl-type substrates **133** and **135**, whereas compound **131** did not react at all. No oxidative coupling was observed with phenolic benzyl alcohols.

Oxidation of more complex, dimeric lignin model compounds was studied as well. The phenolic model compound **141** yielded the C–C coupled tetrameric compound **143** quantitatively; no oxidation of benzylic OH to ketone was observed. The non-phenolic model compound **142** was nonreactive under the conditions studied. A model compound for lignin chromophores, stilbene **144**, was oxidised to the corresponding diol **145**, most likely *via* an epoxide, by using manganese complex as catalyst and H_2O_2 as oxidant. When compound **144** was oxidised with dioxygen catalysed by cobalt complex, vanillin was identified as the main product.

Finally, study was made of the effect of electron withdrawing and electron donating substituents in Mn(salen) derivatives used to catalyse the oxidation of simple phenol, 2,5-di-*tert*-butylhydroquinone **146**, to corresponding 2,5-di-*tert*-butyl-1,4-benzoquinone **147**. The rate of the reaction was followed by UV-Vis spectrometry. Contrary to findings for alkene epoxidation and

oxidation of sulfides to sulfoxides, presence of the electron withdrawing substituents in the catalyst was found to decrease the reaction rate.

The amphiphilic complexes derived from ligands **70** and **71** could potentially be used as catalysts for a wide range of reactions, in both organic and aqueous media. Study of the chiral complexes with ligand **71** in various asymmetric syntheses would be of interest. The cationic phosphonium groups in these types of complexes should make it easy to immobilise them in solid supports, allowing easy separation from the reaction mixture and possibly recyclability. Complexes **100**-**103**, which displayed high activity as oxidation catalysts, might be modified to prepare chiral analogues, for example for use as catalysts in the asymmetric oxidation of benzylic hydrocarbons.

7. EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 2000 operating at 200.0 and 50.0 MHz, respectively. Residual solvent signals were used as references. 1,4-Dioxane was used as an internal standard with D_2O. EI mass spectra were obtained using a JEOL JMS-SX102 spectrometer. ESI mass spectra were obtained using a PerSeptive Biosystems Mariner Biospectrometry Workstation ES-TOF spectrometer operating at positive-ion mode in acetonitrile–H_2O (1:1) containing 10 mmol NH_4OAc at pH 7.5 or in MeOH–H_2O (1:1). Elemental analyses were conducted at University of Helsinki, Department of Pharmacy, using a CE-Instruments Eager EA 1110 instrument. FTIR spectra were recorded from neat samples pressed against a diamond window using a Perkin-Elmer Spctrum One spectrometer. Melting points were measured using an Eloctrothermal apparatus in open glass capillaries and are uncorrected.

7.1. Synthesis of 5,5'-substituted salen complexes

Ligands for the complexes **83**-**86**, **88**, **90**-**93** and **95** were synthesised by the standard method.[17] Ligands for the sulfonated complexes were prepared by a modified literature method.[44] Manganese complexes **83**-**86** and **88** were synthesised by the published procedure.[V] Sulfonated complex **87** was synthesised by refluxing equimolar amounts of the corresponding ligand and $Mn(OAc)_2 \cdot 4H_2O$ in 80% EtOH for 3 h and filtering out the product. The product was washed successively with 80% EtOH, EtOH and Et_2O.

Cobalt complexes **90**-**93** and **95** were synthesised by refluxing an EtOH solution of the ligand and 2 eq. of $Co(OAc)_2 \cdot 4H_2O$ for 2 h, adding water and filtering out the product. The product was washed successively with water, 80% EtOH and Et_2O. Sulfonated complex **94** was prepared like the manganese complex **87**.

Ligand 148, 2,2'-[1,2-Ethanediylbis(nitrilomethylidyne)]bis[4-methoxyphenol]

Yellow powder, yield 84%. $\delta_H(CDCl_3)$ 3.74 (6 H, s), 3.92 (4 H, s), 6.72–6.73 (2 H, m), 6.89-6.90 (4 H, m), 8.29 (2 H, s), 12.70 (2 H, br s); $\delta_C(CDCl_3)$ 55.93, 59.86, 114.94, 117.70, 118.27, 119.53, 152.04, 155.15, 166.28; HRMS (EI) *m/z* found 328.1428, calc. for $C_{18}H_{20}O_4N_2$ 328.1423.

Ligand 149, 2,2'-[1,2-Ethanediylbis(nitrilomethylidyne)]bis[4-methylphenol]

Yellow plates, yield 90%. $\delta_H(CDCl_3)$ 2.26 (6 H, s), 3.92 (4 H, s), 6.83–7.12 (6 H, m), 8.30 (2 H, s), 12.98 (2 H, br s); $\delta_C(CDCl_3)$ 20.35, 59.90, 116.70, 118.33, 127.74, 131.57, 133.21, 158.78, 166.49; HRMS (EI) *m/z* found 296.1535, calc. for $C_{18}H_{20}O_2N_2$ 296.1525.

Ligand 150, 2,2'-[1,2-Ethanediylbis(nitrilomethylidyne)]bis-phenol

Yellow plates, yield 98%. $\delta_H(CDCl_3)$ 3.93 (4 H, s), 6.80–7.03 (6 H, m), 8.30 (2 H, s), 13.02 (2 H, br s); HRMS (EI) *m/z* found 268.1206, calc. for $C_{16}H_{16}N_2O_2$ 268.1208.

Ligand 151, 2,2'-[1,2-Ethanediylbis(nitrilomethylidyne)]bis[4-bromophenol]

Yellow plates, yield 95%. $\delta_H(CDCl_3)$ 3.95 (4 H, s), 6.83–6.87 (2 H, m), 7.35–7.39 (4 H, m), 8.29 (2 H, s), 13.14 (2 H, s); $\delta_C(CDCl_3)$ 59.69, 110.27, 113.49, 119.13, 133,64, 135.25, 160.12, 165.41; HRMS (EI) *m/z* found 423.9419, calc. for $C_{16}H_{14}Br_2O_2N_2$ 423.9418.

Ligand 152, 2,2'-[1,2-Ethanediylbis(nitrilomethylidyne)]bis[4-sulfonatophenol] disodium salt

Light yellow fluffy powder, yield 91%. $\delta_H(D_2O)$ 3.86 (4 H, s), 6.61 (1 H, d, *J*=10.8 Hz), 7.50–7.58 (2 H, m), 8.25 (2 H, s); MS (ESI) *m/z* found 473.1, calc. for $C_{16}H_{15}N_2Na_2O_8S_2$ $[M + H]^+$ 473.0.

Ligand 153, 2,2'-[1,2-Ethanediylbis(nitrilomethylidyne)]bis[4-nitrophenol]

Orange powder, yield 90%. $\delta_H(DMSO–d_6)$ 4.04 (4 H, s), 6.52–6.60 (2 H, m), 7.59–7.63 (2 H, m), 7.99–8.03 (2H, m), 8.67 (2 H, s), 14.52 (2 H, br s); $\delta_C(DMSO–d_6)$ 52.55, 112.20, 119.30, 132.24, 140.41, 164.67, 168.10; HRMS (EI) *m/z* found 358.0916, calc. for $C_{16}H_{14}N_4O_6$ 358.0910.

Complex 83

Brown powder, yield 88%. HRMS (EI) *m/z* found 418.0298, calc. for $C_{18}H_{18}ClMnN_2O_4$ 418.0301.

Complex 84

Brown powder, yield 81%. HRMS (EI) *m/z* found 386.0410, calc. for $C_{18}H_{18}ClMnN_2O_2$ 386.0403.

Complex 85

Dark brown crystals, yield 85%. HRMS (EI) *m/z* found 358.0101, calc. for $C_{16}H_{14}ClMnN_2O_2$ 358.0091.

Complex 86

Brown powder, yield 91%. HRMS (EI) *m/z* found 513.8305, calc. for $C_{16}H_{12}Br_2ClMnN_2O_2$ 513.8301.

Complex 87

Light brown fluffy powder, yield 80%. MS (ESI) *m/z* found 527.9, calc. for $C_{16}H_{13}MnN_2Na_2O_8S_2$ $[M + H]^+$ 527.9.

Complex 88

Orange-brown powder, yield 93%. HRMS (EI) *m/z* found 447.9800, calc. for $C_{16}H_{12}ClMnN_4O_6$ 447.9793.

Complex 90

Dark brown powder, yield 82%. HRMS (EI) *m/z* found 385.0595, calc. for $C_{18}H_{18}CoN_2O_4$ 385.0599.

Complex 91

Dark brown powder, yield 87%. HRMS (EI) *m/z* found 353.0696, calc. for $C_{18}H_{18}CoN_2O_2$ 353.0701.

Complex 92

Brownish-black powder, yield 90%. HRMS (EI) *m/z* found 325.0388, calc. for $C_{16}H_{14}CoN_2O_2$ 325.0389.

Complex 93

Dark brown powder, yield 96%. HRMS (EI) *m/z* found 480.8591, calc. for $C_{16}H_{12}Br_2CoN_2O_2$ 480.8599.

Complex 94

Dark brown fluffy powder, yield 74%. MS (ESI) *m/z* found 532.0, calc. for $C_{16}H_{13}CoN_2Na_2O_8S_2$ $[M + H]^+$ 531.9.

Complex 95

Brown powder, yield 83%. HRMS (EI) *m/z* found 415.0099, calc. for $C_{16}H_{12}CoN_4O_6$ 415.0091.

Complex 82

Aldehyde **99** (0.50 g, 3.03 mmol) was dissolved in refluxing EtOH (10 ml). Ethylenediamine (90 mg, 1.52 mmol) was added, giving a red solution. After 15 min, $Mn(OAc)_2 \cdot 4H_2O$ (0.74 g, 3.02 mmol) was added. The brown solution was refluxed for 1 h, LiCl (0.19 g, 4.48 mmol) was added and the refluxing was continued for 3 h. The black reaction mixture was concentrated to 5 ml and water (5 ml) was added. The solution was cooled and the product was filtered out and washed with water and 70% EtOH; a very dark brown powder (0.49 g, 73%) was obtained. According to mass spectral study, the product was impure, consisting of two unidentified compounds in addition to **82**.

Complex 89

Complex **89** was prepared like complex **82**, but with use of $Co(OAc)_2 \cdot 4H_20$ instead of $Mn(OAc)_2 \cdot 4H_2O$ and without the addition of LiCl. Black powder, yield 77%. Like complex **82**, this complex was impure.

7.2. Synthesis of aldehyde 99

Compound 97

2-Hydroxy-5-nitrobenzaldehyde **96** (3.56 g, 21.3 mmol), 2,2-dimethyl-1,3-propanediol (4.44 g, 42.6 mmol) and *p*-TsOH (0.10 g, 0.5 mmol) were dissolved in toluene (25 ml). The mixture was refluxed under a Dean-Stark apparatus for 2 h. The mixture was cooled, EtOAc (30 ml) was added and the solution was washed successively with saturated $NaHCO_3$ solution (2 × 20 ml), water (3 × 50 ml) and brine (30 ml). After the organic phase was dried with Na_2SO_4 and evaporated, it yielded a yellowish solid (3.95g, 73%). $\delta_H(CDCl_3)$ 0.85 (3 H, s), 1.28 (3 H, s), 3.68–3.89 (4 H, m), 5.62 (1 H, s), 6.93–6.98 (1 H, m), 8.11–8.18 (2 H, m), 8.84 (1 H, br s); $\delta_C(CDCl_3)$ 21.85, 23.09, 30,36, 77.90, 95.80, 119,84, 125.69, 129.30, 135.72, 152.57. No molecular ion was detected in EI mass spectra.

Compound 99

Compound **97** (3.80 g, 15.0 mmol), formalin (37%, 10 ml, 123.2 mmol of formaldehyde), Pt_2O (40 mg, 0.18 mmol) and 10% Pd/C (0.44 g) were added to THF–EtOH (1:2, 60 ml). The mixture was vigorously stirred under H_2 (atmospheric pressure) until about 2000 ml of H_2 was consumed. The reaction mixture was filtered and the filtrate was evaporated to dryness; **98** was obtained as a yellowish oil (2.99 g, 79%). $\delta_H(CDCl_3)$ 2.65 (6 H, s), 3.65–3.80 (4 H, m), 5.70 (1 H, s), 6.20 (1 H, br s), 6.82–7.29 (3 H, m); $\delta_C(CDCl_3)$ 21.77, 22.95, 30.20, 44.69, 77.68, 98.95, 119.57, 120.75, 123.11, 140.69, 148.79. No molecular ion was detected in the EI mass spectra. The residue was

dissolved in EtOAc (30 ml) and washed with water (3 × 20 ml). The organic phase was extracted with 2M HCl (3 × 10 ml). The combined extracts were neutralised with saturated Na_2CO_3 solution and extracted with CH_2Cl_2 (4 × 15 ml). The combined organic extracts were washed with water (20 ml) and brine (20 ml) and dried with Na_2SO_4. The dark-coloured solution was treated with activated carbon, filtered through a Celite pad and evaporated to dryness. The residue was dissolved in EtOAc–hexane (1:1, 50 ml) and filtered through a short silica gel column. Evaporation of the solvent gave an orange oil (1.71 g, 69%). $\delta_H(CDCl_3)$ 2.85 (6 H, s), 6.91–7.22 (3 H, m), 9.90 (1 H, s), 11.56 (1 H, br s); $\delta_C(CDCl_3)$ 42.87, 119.80, 120.60, 123.22, 124.59, 125.97, 154.91, 196.96; HRMS (EI) *m/z* found 165.0784, calc. for $C_9H_{11}NO_2$ 165.0787.

7.3. Synthesis of complexes 100-103

2-Hydroxy-3-(3-imidazol-1-ylpropoxy)benzaldehyde **109** was synthesised by a literature method.[71] 2-Hydroxy-3-(3-imidazol-1-ylbutoxy)benzaldehyde **110** was prepared by the same method. Data for **110**: $\delta_H(CDCl_3)$ 1.79–2.07 (4 H, m), 4.02–4.12 (4 H, m), 6.90–7.26 (5 H, m), 7.52 (1 H, s), 9.91 (1 H, s), 10.83 (1 H, s); $\delta_C(CDCl_3)$ 26.1, 28.3, 46.7, 70.0, 118.8, 119.6, 119.9, 125.2, 129.5, 137.2, 147.6, 152.0, 196.6; (HRMS, EI) *m/z* found 260.1150, calc. for $C_{14}H_{16}N_2O_3$ 260.1161; MS (EI) *m/z* 261 ($[M+1]^+$, 12%), 260 (M^+, 68), 232 (100), 215 (23), 203 (21), 137 (10), 123 (64), 110 (17), 96 (52), 81 (34), 68 (26), 55 (12).

Synthesis of ligand 113

2-Hydroxy-3-(3-imidazol-1-ylpropoxy)benzaldehyde **109** (236 mg, 0.96 mmol) was dissolved in absolute EtOH (5 ml) with warming. To the stirred solution was added ethylenediamine (29 mg, 0.48 mmol). The yellow solution turned orange, and was refluxed for 2 h, after which the colour was again bright yellow. To the hot mixture was added diisopropyl ether until it was slightly turbid. After storing in a refrigerator over the weekend, the bright yellow product was filtered off and

washed with diisopropyl ether. Recrystallisation from 2-propanol yielded **113** as bright yellow, small plates (198 mg, 80%). mp 162–163 °C (from 2-propanol); $\delta_H(CDCl_3)$ 2.18–2.30 (4 H, m), 3.94 (4 H, t, *J*= 5.6 Hz), 3.97 (4 H, s), 4.24 (4 H, t, *J*=6.7 Hz), 6.71–7.04 (10 H, m), 7.51 (2 H, s), 8.37 (2 H, s), 13.66 (2 H, s); $\delta_C(CDCl_3)$ 30.8, 43.3, 59.4, 65.3, 117.0, 118.1, 119.0, 124.1, 127.5, 129.5, 137.5, 147.0, 152.0, 166.6; MS (ESI) *m/z* found 534.3, calc. for $C_{28}H_{36}N_7O_4$ $[M+NH_4]^+$ 534.3.

Synthesis of ligand 114

2-Hydroxy-3-(3-imidazol-1-ylbutoxy)benzaldehyde **110** (0.50 g, 1.92 mmol) was dissolved in absolute ethanol (10 ml) with warming. To the stirred solution was added ethylenediamine (58 mg, 0.97 mmol). The yellow solution turned orange and was refluxed for 2.5 h. The solvent was evaporated off and the residue was chromatographed on Et_3N-neutralised silica gel ($CHCl_3$–EtOH, 1:0–5:1 gradient). Ligand **114** was obtained as an orange-yellow oil that formed a sticky solid on prolonged standing (324 mg, 62%). $\delta_H(CDCl_3)$ 1.77–1.83 (4 H, m), 1.86–2.08 (4 H, m), 3.94 (4 H, s), 3.99–4.06 (8 H, m), 6.70–7.03 (10 H, m), 7.53 (2 H, s), 8.33 (2 H, s), 13.58 (2 H, s); $\delta_C(CDCl_3)$ 26.2, 28.5, 46.8, 50.7, 59.5, 68.7, 116.0, 118.1, 118.9, 123.7, 129.3, 137.2, 147.3, 151.8, 166.6; MS (ESI) *m/z* found 562.3, calc. for $C_{30}H_{40}N_7O_4$ $[M+NH_4]^+$ 562.3; MS (EI) *m/z* 544 (M^+, 3%), 277 (40), 262 (100), 183 (43), 123 (17), 108 (15), 91 (12), 68 (11).

Syhthesis of monoimine 111

The literature method was followed in the synthesis.[219] Compound **111** was isolated from the product mixture by dry-column chromatography on silica gel [diimine **112** was eluted first with EtOAc–hexane (2:1), and then **111** with acetone–MeOH (10:1)]. Compound **111** was obtained as a yellow oil that solidified slowly in the refrigerator to a sticky solid (380 mg, 26%). $\delta_H(CDCl_3)$ 0.86–1.98 (11 H, m), 3.31–3.35 (1 H, m), 6.76–6.91 (2 H, m), 7.14–7.25 (2 H, m), 8.27 (1 H, s),

13.25 (1 H, br s); δ_C($CDCl_3$) 24.2, 33.1, 42.5, 54.0, 72.6, 91.0, 116.7, 118.6, 131.5, 132.1, 141.2, 160.9, 164.7; HRMS (EI) *m/z* found 218.1416, calc. for $C_{13}H_{18}N_2O$ 218.1419.

Synthesis of ligand 115

Monoimine **115** (160 mg, 0.73 mmol) was dissolved in absolute EtOH (15 ml). To this solution was added 2-hydroxy-3-(3-imidazol-1-ylpropoxy)benzaldehyde **109** (181 mg, 0.73 mmol) and the orange mixture was heated to reflux. The mixture turned yellow and was refluxed for 3 h. The solvent was evaporated off and the residue filtered through a short Et_3N-neutralised silica gel column [$CHCl_3$–EtOH (5:1)]. Ligand **115** was obtained as an orange-yellow oil (285 mg, 87%). δ_H($CDCl_3$) 1.43–2.04 (8 H, m), 2.19–2.31 (2 H, m), 3.30–3.40 (2 H, m), 3.93 (2 H, t, *J*=5.5 Hz), 4.25 (2 H, t, *J*=6.7 Hz), 6.66–7.24 (10 H, m), 7.53 (1 H, s), 8.27 (1 H, s), 13.87 (2 H, br s); δ_C($CDCl_3$) 24.1, 30.9, 33.0, 43.4, 45.8, 65.1, 72.2, 72.3, 72.6, 116.5, 116.7, 117.9, 118.6, 118.7, 119.0, 124.1, 129.3, 131.4, 132.2, 137.4, 147.0, 152.2, 152.3, 160.9, 164.7 (2 overlapping peaks); HRMS (EI) *m/z* found 446.2327, calc. for $C_{26}H_{30}N_4O_3$ 446.2318; MS (EI) *m/z* 447 ($[M+1]^+$, 37 %), 446 (M^+, 100), 351 (15), 325 (42), 246 (41), 201 (17), 122 (22), 82 (34).

Synthesis of ligand 116

Ligand **116** was prepared like **115** using monoimine **111** (210 mg, 0.96 mmol) and 2-hydroxy-3-(3-imidazol-1-ylbutoxy)benzaldehyde **110** (250 mg, 0.96 mmol) in absolute EtOH (20 ml). The product was obtained as an orange-yellow oil (394 mg, 86%). δ_H($CDCl_3$) 1.47–2.06 (12 H, m), 3.30–3.34 (2 H, m), 3.98–4.10 (4 H, m), 6.66–7.24 (9 H, m), 7.55 (1 H, s), 8.26 (2 H, s), 13.31 (1 H, br s), 13.82 (1 H, br s); δ_C($CDCl_3$) 24.1 (2 overlapping peaks), 26.1, 28.3, 33.0, 46.7, 68.4, 72.3 (2 overlapping peaks), 72.6 (2 overlapping peaks), 115.5, 116.7, 117.8, 118.5, 118.8, 123.5, 129.2, 131.4, 132.1, 137.2, 144.6, 147.3, 151.9, 160.9, 164.6 (2 overlapping peaks); HRMS (EI) *m/z* found

460.2482, calc. for $C_{27}H_{32}N_4O_3$ 460.2474; MS (EI) *m/z* 461 ($[M+1]^+$, 33%), 460 (M^+, 100), 339 (37), 322 (23), 260 (43), 258 (19), 245 (10), 201 (38), 183 (10), 122 (63), 116 (24).

Synthesis of complexes 100 and 101

Complexes **100** and **101** were synthesised by the same method. Synthesis of **100** is given as an example. Ligand **113** (200 mg, 0.387 mmol) was dissolved in absolute EtOH (6 ml) with warming. $Mn(OAc)_2{\cdot}4H_20$ (98 mg, 0.387 mmol) was added as a solid. The mixture immediately turned from yellow to dark brown and was refluxed for 1.5 h. The solution was allowed to cool somewhat, Et_2O (15 ml) was added and the mixture was cooled in a refrigerator for a few hours. The precipitated complex was filtered off and washed with Et_2O. When the product was recrystallised by diffusing a MeOH solution of the crude complex to EtOAc, complex **100** was obtained as dark brown crystals (205 mg, 82%). mp 123–124 °C (from MeOH–EtOAc); Found: C, 56.3; H, 5.9; N, 12.2, $C_{33}H_{42}MnN_6O_7$ (**100**·EtOAc·MeOH) requires C, 57.5; H, 6.1; N, 12.2 %; ν_{max}/cm^{-1} 3255 (MeOH), 1621 (C=N); MS (ESI) *m/z* found 587.2, calc. for $C_{28}H_{34}MnN_7O_4$ $[M+NH_4]^+$ 587.2.

Complex 101: Brown powder, yield 91%. mp 155–156 °C (from MeOH–EtOAc); Found: C, 56.4; H, 6.0; N, 11.1. $C_{35}H_{46}MnN_6O_7$ (**101**·EtOAc·MeOH) requires C, 58.6; H, 6.5; N, 11.7 %; ν_{max}/cm^{-1} 3266 (MeOH), 1619 (C=N); MS (ESI) *m/z* found 615.2, calc. for $C_{30}H_{38}MnN_7O_4$ $[M+NH_4]^+$ 615.2.

Synthesis of complexes 102 and 103

Complexes **102** and **103** were synthesised by the same method. Synthesis of **102** is given as an example. Ligand **115** (260 mg, 0.58 mmol) was dissolved in absolute EtOH (5 ml) with warming. $Mn(OAc)_2{\cdot}4H_2O$ (150 mg, 0.61 mmol) was added as a solid. The mixture immediately turned from yellow to dark brown. This solution was stirred and refluxed for 3 h. The solvent was evaporated and the residue (as an acetate salt) was dissolved in MeOH. To this solution was added a three-fold

excess of NH_4PF_6 in MeOH. Enough MeOH was added to dissolve the precipitate, the resulting mixture was filtered and distilled water was added until the solution was slightly turbid. This was allowed to evaporate at room temperature. The product was filtered out yielding **102** as brown solid (269 mg, 72%); mp 260–262 °C (from MeOH–H_2O); Found: C, 49.2; H, 5.1; N, 8.3, $C_{27}H_{32}F_6MnN_6O_4P$ (**102**·MeOH) requires C, 47.9; H, 4.8; N, 8.3%; ν_{max}/cm^{-1} 1616 (C=N), 1606 (C=N), 839 (PF_6^-); MS (ESI) *m/z* found 662.2, calc. for $C_{26}H_{32}F_6MnN_5O_3P$ $[M+NH_4]^+$ 662.2; found 499.2, calc. for $C_{26}H_{28}MnN_4O_3$ $[M–PF_6]^+$ 499.2.

Complex 103

Brown solid, yield 66%; mp 208–210 °C (from MeOH–H_2O); Found: C, 44.9; H, 5.1; N, 7.2, $C_{27}H_{36}F_6MnN_6O_6P$ (**103**·3H_2O) requires C, 45.5; H, 5.1; N, 7.9%; ν_{max}/cm^{-1} 1618 (C=N), 1604 (C=N), 838 (PF_6^-); MS (ESI) *m/z* found 676.2, calc. for $C_{27}H_{34}F_6MnN_5O_3P$ $[M+NH_4]^+$ 676.2; found 513.2, calc. for $C_{27}H_{30}MnN_4O_3$ $[M–PF_6]^+$ 513.2.

7.4. Oxidation of 146 followed by UV-Vis spectrometry

Absorbance measurements were carried out in 10 mm quartz cuvettes. The absorbance of the reaction mixture was determined at three minute intervals up to 42 min at 288 nm. Solutions for the measurements were made in spectrometric grade MeOH by adding to the MeOH in the cuvette the stock solutions of **146** and catalysts **83**-**88** (2 mol-% relative to **146**) in MeOH. These were mixed, a stock solution of 30% H_2O_2 in MeOH (100 eq. relative to **146**) was added and the final solution was quickly and thoroughly mixed. The absorbance measurements were started immediately. The changes in absorbance in the first three minutes were plotted (Fig. 45) to determine the relative rates of reactions and thus the catalyst activity.

7.5. Oxidation of benzylic hydrocarbons

The substrate (1.0 mmol) and the catalyst **100** (5 mol-%) were mixed in acetonitrile (10 ml). The oxidant (3.0 mmol) was added in three portions at 20 min intervals. The reaction mixture was stirred overnight at room temperature and filtered through a short silica gel plug to remove the catalyst and excess oxidant. The amounts of the oxidised products were determined by NMR spectrometry. Results: ethylbenzene gave 41% acetophenone and 10% 1-phenylethanol; propylbenzene gave 38% propiophenone and 9% 1-phenylpropanol; diphenylmethane gave 85% benzophenone.

7.6. Oxidation of 2,4,6-trichlorophenol

The substrate (1.0 mmol) and catalyst **100** (5 mol-%) were dissolved in aqueous acetonitrile [10 ml, (1:9)]. 30% H_2O_2 (3 eq.) was added and the mixture was stirred at room temperature. After 1 h, the mixture was poured into H_2O (50 ml) and extracted with CH_2Cl_2 (3 × 20 ml). The combined organic extracts were washed with H_2O (20 ml) and brine (20 ml) and dried with Na_2SO_4. The solvent was evaporated off and the purple residue was analysed by NMR spectrometry. Only a minute amount of starting material was left; otherwise the spectra contained very broad signals indicating the formation of coupling products. Low intensity signals for the degradation product 2,6-dichloro-1,4-benzoquinone were also evident in the NMR spectra.

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